Chapter 11
Electrochemical and Magnetic Technologies for Bio Applications

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11.1 Electrochemical and Magnetic Probes for Biochip Applications

The electrochemical and magnetic biosensors have an advantage because of the easy miniaturization of electric device components as compared with photometric instruments. These technologies have been applied to develop portable, compact and inexpensive biochip devices. A commercially successful example is the glucose sensor using enzyme transducers, which was originally reported by Clark and Lyons [1] to measure glucose by detecting the decrease in oxygen by pO_2 electrode when glucose is converted to gluconic acid and hydrogen peroxide. Electrochemical biosensors can be separated into three typical assay systems using amperometric, potentiometric or conductometric transducers. Furthermore, various magnetosensors using magnetic particles have been developed over a decade in place of photometric biosensors. In this chapter, recent advances in electrochemical and magnetic biosensors toward development of portable, compact and inexpensive biochip devices have been focused.

Electrochemical biosensors have been divided into two basic types: enzyme-based sensor and electrochemical probe-based sensor. Alkaline phosphatase (ALP) and horse radish peroxidase (HRP) have been often employed for enzyme-based biosensors using p-nitrophenyl phosphate (PNP), α-naphtyl phosphate, 3–3′,5,5′-tetramethylbenzidine (TMB) and 2,2′-azino-bis-(3-ethylbenzthiazoline-6-sulfonic acid) (ABTS) as substrates of electrochemically active species, and ferrocene (Fc) and methylene blue as the electrochemical mediators. In general, enzymatic amplification of electrochemical signals enables highly sensitive detection of analytes. On the other hand, a direct detection of analytes by using electrochemical probes allows a more rapid time-response onto the detector surface and needs no enzymatic reaction. Based on the reason, a direct detection of analytes by using electrochemical probes has been

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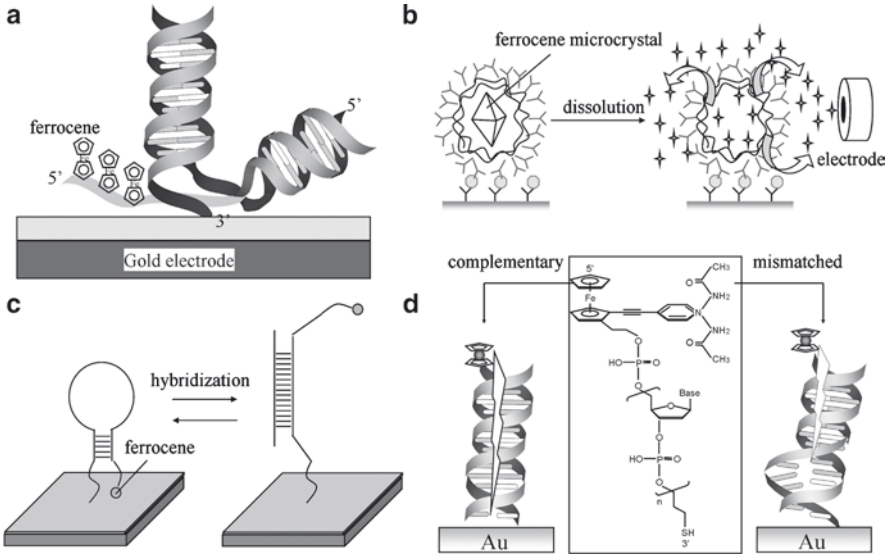

Fig. 11.1 Direct detection of electrochemical signals using ferrocene-labeled biomolecules. Adapted from (**a**) Umek et al. 2001; (**b**) Mak et al. 2005; (**c**) Fan et al. 2003; (**d**) Inouye et al. 2005

preferred to simplify the process towards miniaturized biochip devices. A CMOS-based electric DNA chip, eSensor™ with 16 gold electrodes manufactured by printed circuit board technology has been developed [2]. Thiolated oligonucleotide probes are immobilized directly onto the gold electrode surface. The detection of DNA hybridization is performed by alternating current voltametry using ferrocene-incorporated oligonucleotides as detection probes (Fig. 11.1a) [3]. However, the study of electrochemical probe-based biosensors has been limited by the sensitivity as compared with enzyme-based biosensors. To overcome the limitation, various approaches have been attempted.

Various probes for the electrochemical detection have been reported, such as ferrocene [4, 5], gold nano particles [6], intercalater [7] and semiconductor nanoparticles [8]. Among them, ferrocene derivatives have often been used as electrochemical probes for immunoassay [9–11] as well as the DNA hybridization assay [4, 5, 12–14]. Labeling of ferrocene derivatives to enzymes such as glucose oxidase has been intensively studied and used as mediators in biosensors [15–17]. Also, electroactive labeling of IgG with ferrocenemonocarboxylic acid (Fc-COOH) by chemical crosslinkers, sulfo-N-hydroxysulfosuccinimide (NHS) and 1-ethyl-3-[3-dimethylaminopropyl]-carbodiimide hydrochloride (EDC), has been commonly used [9, 10] (Fig. 11.2a). Only two to three ferrocene moiety have been stably introduced to IgG. Recently, labeling of ferrocenecarboaldehyde (Fc-CHO) to immunoglobulin G (IgG) via formation of Schiff-base and its reduction was investigated for construction of an electrochemical probe for miniaturized amperometric flow immunoassay [18] (Fig. 11.2b). Approximately, eight molecules of Fc–CHO

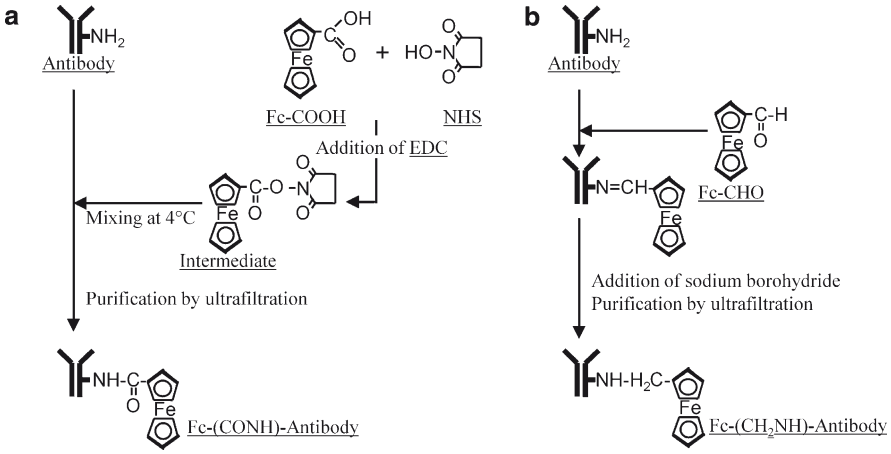

Fig. 11.2 Reaction schemes for labeling of IgG with ferrocenemonocarboxylic acid (Fc-COOH) (**a**) and ferrocenecarboaldehyde (Fc-CHO) (**b**)

were labeled to IgG and the reversible redox property of ferrocene was observed. Labeling efficiency improved by over three times as compared to the conventional method using ferrocenemonocarboxylic acid (Fc–COOH). IgG labeled with Fc–CHO that retained eight ferrocene moiety showed sufficient binding affinity to its antigen and the current response obtained in the flow electrochemical detection system increased by 14-fold as compared with IgG labeled with Fc–COOH. The minimum detectable concentration of IgG labeled with Fc–CHO was 60 pM. IgG labeled with Fc–CHO demonstrate biochemical and electrochemical properties, which are useful for electrochemical immunosensors (See also section 11.2). The utilization of encapsulated ferrocene microcrystal was proposed as another approach to increase the electroactive species in probe-based immunosensors (Fig. 11.1b) [19]. Ferrocene microcrystals encapsulated within a capsule, which provided a stable interface for antibody conjugation, were used as an electrochemical probe to perform a sandwich immunoassay. After the immunoreaction with ferrocene microcrystal-antibody complexes, the dissolution of the ferrocene microcrystals, and subsequent amperometric detection of the released ferrocene molecules were performed. The ferrocene microcrystal-based biosensor provided a high-signal molecule to antibody ratio of 10^4–10^5 (detection limit: 20 pM).

The direct detection of DNA via conformational changes of ferrocene-conjugated DNA stem-loop (or hair-pin) structure onto electrode surface induced by the hybridization was also proposed (Fig. 11.1c) [4, 20]. The conformational change induces the displacement of ferrocene molecules from the electrode surface, resulting in a drop in peak redox current measured by cyclic voltametry. The detection limits were 115 fM for 24-base oligonucleotide [20] and 10 pM for 17-base oligonucleotide [4], respectively. Furthermore, the difference between

chemical structures of ferrocene-conjugated DNA hybridized with a complementary or a single-base mismatch was detected by hole transport (Fig. 11.1d). The presence of a single-base mismatch in the DNA duplexes caused a dramatic decrease in the electrochemical response [21].

Alternative approach for direct detection is magnetosensor. Magnetic particles are useful magnetosensor probes for quantitative detection of molecular interactions, including those between antigen-antibody, DNA–DNA and ligand-receptor. Measurements are traditionally performed using superconducting quantum interference device (SQUID) magnetometer [22–25], giant magneto-resistive (GMR) sensors [26–30], magnetic susceptometry [31–34] or magnetic force microscopy [35, 36]. The use of magnetic particles offers a great advantage for assays, because it allows the analytical signal to be measured in terms of intensity of magnetization. Furthermore, the use of magnetic particles enables separation of a trace amount of target in solution, which simplifies the process of sample preparation. These types of magnetosensors are highly sensitive and theoretically can detect single magnetic particles [27]. An ideal magnetic probe for use as a magnetosensor requires uniformity in size and magnetization. Ferromagnetic particles have been used rather than ferrimagnetic particles, since ferrimagnetic particles aggregate with each other in aqueous conditions. The ferromagnetic particles generally used consist of polymer containing dispersed nano-sized magnetic particles, such as maghemite (γ-Fe_2O_3) or magnetite (Fe_3O_4), and have highly uniform diameters. However, they are not sufficiently uniformly magnetic to be used as highly sensitive magnetosensor because of the variation of density of nano-sized magnetic particles [26]. For highly sensitive assay using magnetosensors, it is necessary to use homogenously sized magnetic particles. Furthermore, micro size magnetic particles or aggregates of nano size magnetic particles have been mainly used as magnetosensors. The detection of a single magnetic probe using small magneto-resistive spin valve sensor has been reported. The size of magnetic particle used was, however, micro size (2 μm) and the detection range was narrow, 6–20 particles were needed for magnetic signal detection [30]. These particles are too large for use as probes in place of fluorescent dyes or luminescent reagents. Therefore, the use of nano-sized magnetic particle as a magnetic probe is a preferable approach to develop a novel magnetosensor toward the miniaturization.

Magnetite (Fe_3O_4) particles synthesized by magnetotactic bacteria [37, 38], are more uniform in size and shape as compared with artificial magnetite particles. The bacterial magnetite particles (BacMPs) are small in size (50 to 100 nm) and consist of single crystal of magnetite having a single magnetic domain. Therefore, BacMPs are regarded as having uniform particle size and magnetization. Each BacMP is covered with a lipid bilayer membrane mainly of phosphatidylethanolamine. BacMPs are ferrimagnetic; however, they have excellent dispersion in aqueous solutions imparted by the lipid membrane [39]. The BacMPs have been studied with much interest with reference to many engineering applications, such as immunoassay, DNA detection, ligand screening, and cell separation techniques as magnetic carriers [40–45].

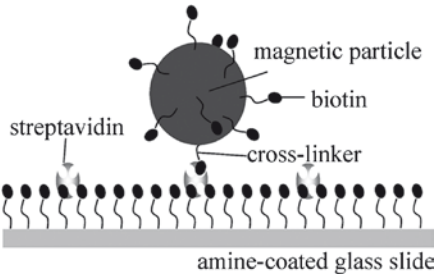

Fig. 11.3 Schematic illustration of biotin-SA interaction on biotinylated glass slide. Biotinylated magnetic particles were applied to the glass slide after treatment with various concentrations of SA

The utilization of BacMPs as a magnetic probe in biosensor has been examined by MFM imaging of single particles [35]. An investigation to determine the presence of a specific biomolecular interaction between biotin and streptavidin (SA) was done using biotinylated BacMPs and biotin-conjugated glass slide (Fig. 11.3). Magnetic detection of SA on biotin-labeled glass slides using biotin-labeled BacMPs was performed by direct BacMP counts using MFM. Biotin-BacMPs were applied to biotin immobilized on the glass slide after treatment with various concentrations of SA. The number of biotin-conjugated BacMPs (biotin-BacMPs) bound to SA immobilized on the glass slides increased with SA concentrations up to 100 pg/ml. The minimum detection limit for SA was 1 pg/ml. For a comparison, a fluorescent detection of Cy3-labeled SA binding onto a biotinylated glass slide was performed by a photomultiplier using a fluorescent scanner. The minimum detection limit of Cy3-SA was 100 pg/ml of SA, which corresponds to approximately 2,000 molecules of SA in the same area if all SA molecules were immobilized on their surface. Fluorescent signals at less than 10 pg/ml SA were not able to discriminate from background noise. This detection limit is almost the same with a previous report (150 pg/ml of IgG) by using a laser-scanning system with a photomultiplier [46]. The results by BacMPs-based assay are 100 times more sensitive for the detection of SA compared with fluorescent detection, thereby suggesting that its use has potential advantages for extremely sensitive biomolecule detection.

11.2 Electrochemical Flow Immunoassay Using Ion Exchange Chromatography

Miniaturized immunosensors, which combine the analytical power of microfluidic devices with the high specificity of antibody-antigen interactions, have been intensively developed [9–11, 47–51]. These platforms have proven to be highly suitable vehicles for conducting various immunoassay protocols. Our research groups have described a new approach to the performance of miniaturized electrochemical flow immunoassay system (on-chip typed flow immunoassay system) by using ferrocene-conjugated

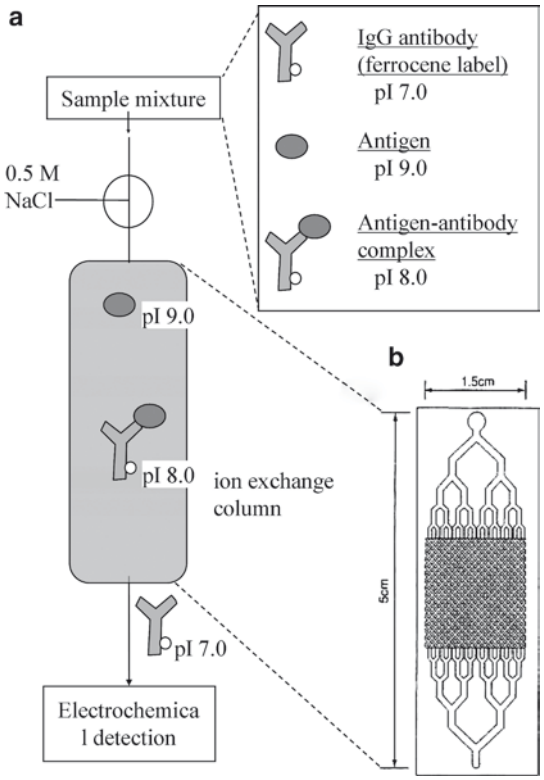

Fig. 11.4 (**a**) Principle of flow immunoassay using ion exchange column. (**b**) Multi-channeled matrix column

antibody as an electrochemical probe and ion exchange chromatography [9, 52] (Fig. 11.4). Antibody-antigen complexes are separated from unreacted antibodies (or antigens) on the basis of their differences in isoelectric point (pI) using an ion-exchange resin, and electrochemically detected using a three-electrode flow-cell system. This method does not require prior immobilization of the antibody onto a solid phase, and has several advantages of a much shorter assay time and a minimal sample volume. Recently, a multi-channeled matrix column coated with cation-exchange resin on PMMA (polymethyl methacrylate) plate, which is the same size as of a credit card, has been constructed as a novel reaction platform towards pregnancy and allergy tests (Fig. 11.4). The flow immunoassay system enables the generation of highly reproducible results using only minute quantities of whole blood samples within 2 min [10]. The integration of chromatography and electrochemical detection with the microchip technology enables us to expand the potentials of other clinical applications, such as diagnosis of diabetes.

Hemoglobin A_{1c} (HbA_{1c}), which is glycated on the N-terminal valine of the β-chain, is well known as the main diabetes marker protein for monitoring long-term glycemic control clinically. Minor hemoglobin (Hb) components including HbA_{1c}

have been originally separated from hemolysates of healthy adult by cation-exchange chromatography [53–55]. Because minor Hb components show lower isoelectric point (pI ; <6.9) than that of non-glycated Hb (HbA_0) due to the glycation [56], they move down a cation-exchange column faster than HbA_0 (pI ; 7.0). HbA_{1c} level in a healthy adult is ranged from approximately 4% to 5.8 % peak area of total Hb on the chromatogram. Based on these understandings, the Japanese Diabetes Society (JDS) has developed a high-resolution cation-exchange chromatography for the detection of HbA_{1c} (KO500 method) [57]. However, the method is time consuming, resulting in slow transfer of examination results from the medical laboratory to the patients. Until now, several POCT devices for simple and rapid HbA_{1c} detection have been proposed to overcome the above problems. In the application for the development of POCT devices, immunoassays are suitable due to the easiness in price-reduction, miniaturization and simplification. However, immunoassay requires an additional process for the evaluation of HbA_{1c} levels because HbA_{1c} levels are expressed as a percentage of total Hb. Total Hb amounts are commonly measured by colorimetry. Because of the difference in detection range between immunoassay and colorimetry, each sample is prepared by individual dilution series. These manual operations should be minimized as far as possible in POCT device for HbA_{1c} to increase the assay precision [58].

In the on-chip typed flow immunoassay system (Fig. 11.5a), manual operation is only mixing the hemolysate sample and ferrocene-conjugated antibody. Although a flow immunoassay system based on boronate affinity for detection of glycated hemoglobin has been proposed [59, 60], ion exchange chromatography is found more suitable to separate and measure each hemoglobin (HbA_0 and HbA_{1c}). This system enables to measure total Hb and HbA_{1c} simultaneously using the same sample. The currents in the eluted fractions were detected by the on-chip typed

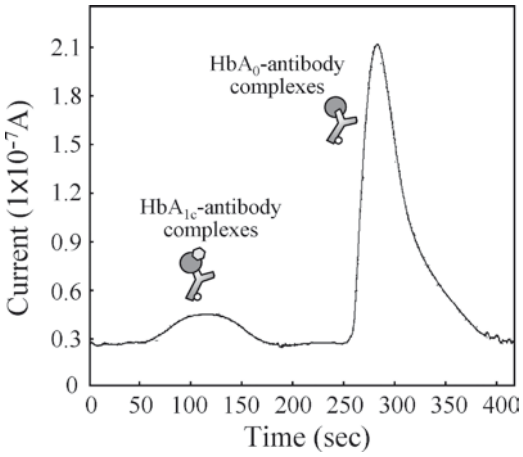

Fig. 11.5 Electrochemical detection of immunocomplexes using on-chip typed cation-exchange chromatography and ferrocene-conjugated antibody. Flow rate: 200 μl/min; Column volume: 30 μl, Buffer change point: 350, 650 s

cation exchange chromatography. Three peaks observed by a stepwise elution, were explained as minor Hbs, HbA_{1c}, HbA_0 and HbA_2. HbA_{1c} levels in hemolysates were calculated from the peak area. Good correlation of HbA_{1c} level between KO500 method and on-chip typed method was obtained (Fig. 11.5b). This method can be applied to POCT devices for clinic or bedside testing of diabetic patients.

11.3 Integrated Genetic Analysis System

Miniaturized biochip device has been recently attracting much attention due to their increasing applications to clinical diagnosis based on genomic analysis, consisting of DNA extraction, PCR, electrophoresis and DNA sequencing (Fig. 11.6). To design a total analysis system on a chip, DNA extraction step plays an important role in subsequent polymerase chain reaction (PCR). Furthermore, microchips to accelerate DNA hybridization and to attain rapid, accurate and high-throughput DNA detection are required. Especially, the detector compatibility with the micro-total analysis system is extremely important to solve the technical and cost problems. In this section, recent developments in DNA extraction and miniaturized photosensor are summarized.

11.3.1 Microchip for DNA Extraction Using Aminosilane-Modified Solid Supports

Magnetic particle (or bead)-based DNA extraction has been commonly used for molecular biology due to quick processing time, reduced chemical need and easy separation using a magnet. Several magnetic particles for DNA extraction have been already commercialized. Magnetic silica particles have been widely used for the DNA extraction based on the method invented by Boom [61]. A solid phase reversible immobilization (SPRI) based on DNA binding to the surface of carboxyl coated solid-phase under conditions of high polyethylene glycol and salt concentration [62, 63] has been developed for a novel DNA purification method specially for highly robust and cost-effective assay toward the complete human genome sequence [64].

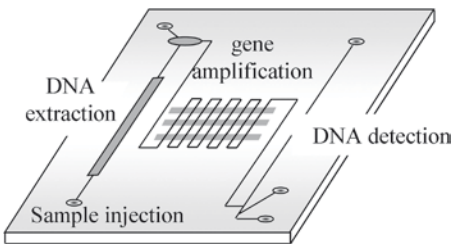

Fig. 11.6 Schematic illustration of integrated genetic analysis system

A separation process using magnetic particles has been commonly accepted as a microdevice or microchamber-friendly procedure. The magnetic separation has been adopted in a number of flow-based analytical operations, such as the purification of PCR products using SA-labeled magnetic particles [65], bound/free separations in immunoassay using antibody-labeled magnetic particles [66] and in pathogen detection using DNA-labeled magnetic particles [67, 68], in microchambers. Despite the utility of magnetic particles, microfabricated structures, such as packed beads, resins and pillars were preferred to magnetic particles [69–71] for flow-based DNA extraction using the Boom method and SPRI, since the magnetic particles settle down by spontaneous sedimentation in aqueous conditions, resulting in the need for suspending magnetic particles in microchamber. Especially, the mixing of magnetic particles in microchamber is difficult for the above-mentioned DNA extraction because highly viscous solutions were used in DNA adsorption process. Until now, the mixing of magnetic particles in a microchamber has not been optimized although several studies on efficient mixing in flat microchamber have been reported in DNA microarray analysis to enhance the hybridization efficiency by using air-driven bladder [72], cavitation microstreaming [73] and chaotic mixer [74]. Furthermore, magnetic particles suitable for flow-based DNA extraction have not been proposed.

Our research groups have demonstrated a novel DNA extraction using aminosilane-modified solid supports [75–77]. The principle is based on electrostatic interaction between amino groups on solid supports and nucleic acids, and subsequent DNA release under high salt or higher pH conditions. In this format, DNA adsorption under high viscous conditions was not required because cell lysates were directly used as DNA samples. At first, a simple microchip device for DNA extraction was constructed based on electrostatic interactions between surface amine groups and DNA. Microchannel (Fig. 11.7a) was fabricated on silicon wafer by photolithography and coated with 3-[2-(2-aminoethylamino)-ethylamino]-propyltrimethoxysilane (AEEA) to introduce amine groups on the surface. The amount of DNA captured in the microchip increased depending on surface amine density. Furthermore, DNA extraction using amine-coated microchip from whole blood was examined. Only DNA was effectively eluted by changing alkalinity of buffer from pH 7.5 to 10.6. The amount of DNA extracted from whole blood was approximately 10 ng and its recovery ratio was 27–40%. Performance of PCR for the eluted fraction indicates that DNA extracted from whole blood was well purified using amine-coated microchip. Recently, a cascading hyperbranched polyamidoamine dendrimer was successfully synthesized on the surface of bacterial magnetic particles (Fig. 11.7B), which were purified from magnetic bacterium, *Magnetospirillum magneticum* strain AMB-1 (See also Section 11.1), to enhance the efficiency of DNA extraction [78, 79]. The amine-dendrimer modified magnetic particles (amine-magnetic particles) show good dispersity in aqueous solutions and easy separation using a magnet after DNA capturing. The high dispersibility will be suitable for an effective mixing of magnetic particles and DNA extraction in microchamber. The potential utility of amine-magnetic particles in the DNA extraction from *Escherichia coli* cells in a polydimethylsiloxane (PDMS)-based microchamber has been investigated. DNA capturing by amine-magnetic particles

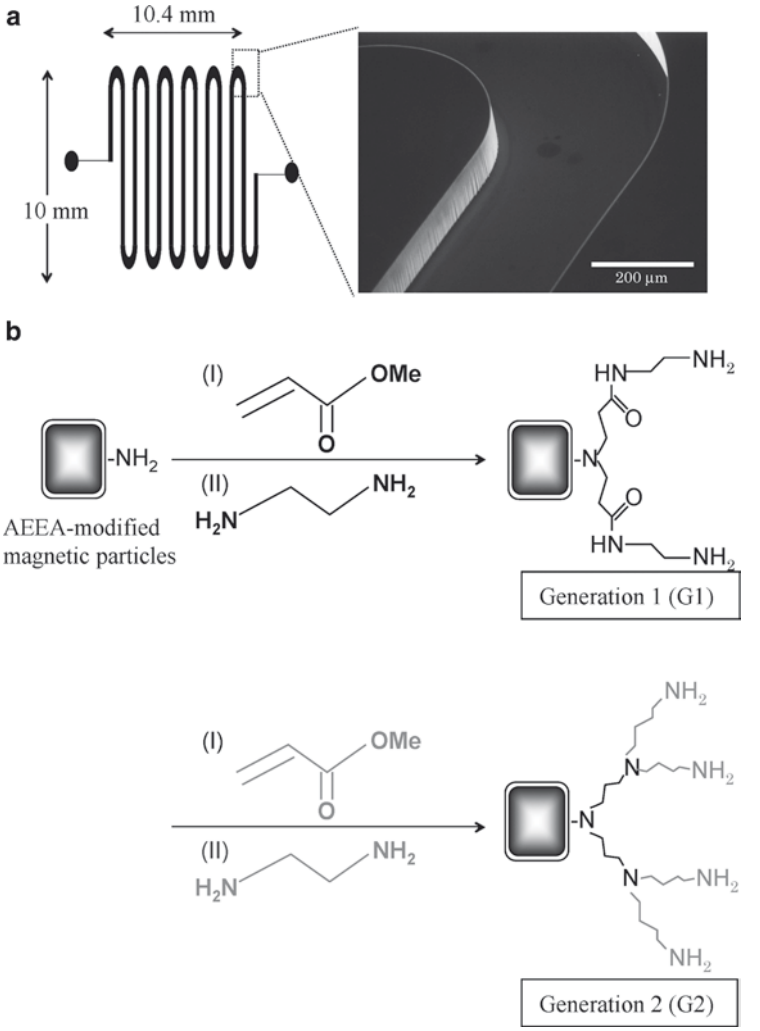

Fig. 11.7 (**a**) Layout of the aminosilane-modified microchip for DNA extraction. Channels: 300 μm wide × 100 μm deep; Total volume: 3.7 μl (adapted from Nakagawa et al. 2005). (**b**) Polyamidoamine dendrimer synthesis on the surface of aminosilane-modified magnetic particles. Dendrimer generation was initiated with AEEA coated magnetic particles in methyl acrylate (I). Then, ethylenediamine (II) was reacted with the modified particles (Generation 1). Stepwise growth was repeated until the desired number of generations was achieved. (adapted from Yoza et al. 2003)

from the cell lysate was more than 90% of released DNA in the PDMS microchamber. These results indicated that efficient cell lysis and DNA capturing was successfully achieved by amine-magnetic particles in the microchamber. Successful PCR amplification was performed using *E. coli* genomic DNA released from amine-magnetic particles. The peak based on PCR amplification was observed by capillary electrophoresis when more than 10^2 cells of *E. coli* were used.

11.3.2 Integrated Circuits for DNA Chip Technology

DNA chips (or microarrays) have been used widely in gene expression studies and genotyping. Photomultiplier tubes (PMTs), which are adopted for use in most commercialized detectors due to their high gain potential (in the order of 10^6) [80], have been one of the preferred detection systems for DNA chips. However, a laser-scanning system and confocal microscopy are required for two-dimensional (2D) measurement of fluorescent spots. Alternatively, charge-coupled device (CCD) arrays have been used for 2D measurements. Recent advances in optical sensing technology allow us to construct compact DNA chip devices. Various photodetectors, such as the PIN photodiode [81, 82], the microavalanche photodiode (μAPD) [83], and the miniature complementary metal oxide semiconductor (CMOS) sensor [84–87] have been proposed in place of PMTs and CCD [88] as they are portable, compact, and inexpensive photodetecting devices, which can be adapted easily to biochip systems. This integrated circuit (IC) technology is a promising technique for DNA chip systems in addition to biochip systems. Electric (or electrochemical) detection of DNA is also a promising technique; however, research on electric DNA sensors has focused more on label-free DNA hybridization [89–93] because electric detection shows good performance at qualitative assays, such as point-of-care testing, but not in quantitative assays as compared with fluorescence detection. In this section, miniaturized photodetectors towards DNA chip technology are summarized (Table 11.1).

In general, DNA probes have not been immobilized directly onto the above photo-detecting devices. Rather, probes have been fixed onto glass slides, optical fibers, membranes, and microchambers as separated reaction sites, because these devices are not disposable and do not have sufficient thermostability under relatively high temperature conditions required for the DNA hybridization and DNA denaturation process. Correspondingly, external optical systems are required to collect the emitted fluorescence efficiently from the separated reaction sites. Thin film transistor (TFT) photosensor was an ideal choice as a disposable and thermostable (tolerant to more than 100°C) photodetecting device [94]. A novel DNA chip system was demonstrated using a TFT photosensor that was fabricated by semiconductor IC technology. The oligonucleotide-arrayed TFT photosensor was applied to single

Table 11.1 Applications of miniaturized photosensor to biosensor

Photosensor	Form at	Application	References
CCD	Luminescence	DNA hybridization	Lamture et al (1994) [88]
PIN photodiode	Fluorescence	Size fractionation of DNA	Kamei et al (2003, 2005) [81, 82]
micro-APD	Fluorescence	–	Chabinyc et al (2001) [83]
CMOS	Fluorescence	–	Vo-Dinh et al (1999) [85]
	Luminescence	Glucose sensor	Ho et al. (2007) [87]
	Luminescence	DNA chip	Mallard et al (2005) [86]
IFT	Fluorescence	DNA chip	Tanaka et al (2006) [94]

nucleotide polymorphisms (SNPs) detection. A SNP in the aldehyde dehydrogenase 2 (ALDH2) gene on chromosome 12, which has significant implications for the evaluation of susceptibility of human organs to damage induced by alcohol [95, 96] was used as a target. DNA hybridization with biotinylated DNA and subsequent binding of fluorescently labeled SA was detected on the TFT photosensor surface. The TFT photosensor consisted of a 200×240 pixel array (50 μm×50 μm each) with a 50-μm pitch. To develop a photosensing system with optimized performance, the spectral responses of the TFT photosensor were measured. The non-coated TFT photosensor detected light over a broad wavelength range with peak sensitivity at 450 nm. A TFT photosensor with a cut-off wavelength shorter than approximately 300 nm was prepared by coating with TiO_2 film. Correspondingly, the wavelength of the excitation source was set at 11 nm below the cut-off wavelength to eliminate excitation light and to detect only the emission radiation on the TFT photosensor (Fig. 11.8a). The UV light source with a band pass filter of 289 nm and cut-off filters for more than 300 nm and 350 nm was used as excitation source. Two fluorophores, AlexaFlour 350 (ex: 346 nm, em: 442 nm) and Qdot 565

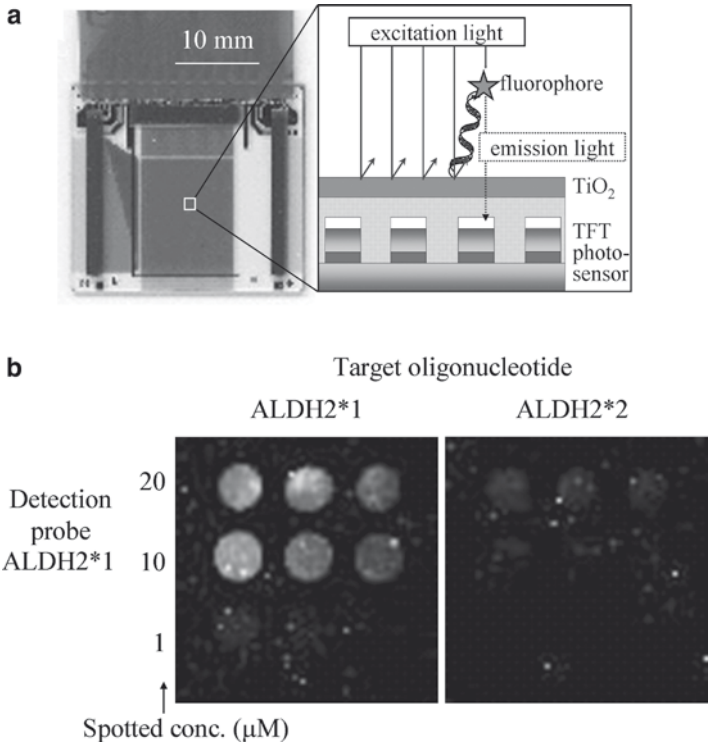

Fig. 11.8 (**a**) Topside view and schematic cross-sectional view of the TFT photosensor. (**b**) TFT photosensor images of oligonucleotide array. Oligonucleotides immobilized on TFT photo sensor were reacted with biotin-labeled ALDH2*1 (21 mer), and subsequently reacted with Alexa Fluor 350-labeled SA. Spot diameter: 500–600 μm

(ex: <565 nm, em: 565 nm) were selected for use because these fluorophores have shorter excitation wavelengths and showed little overlap of the emission signal with the excitation signal. Alexa Fluor 350 is the only organic fluorescent dye, which is commercially available, excited in the ultraviolet wavelength, and shows little overlapping of the emission signal with the excitation signal. DNA hybridization with biotinylated DNA and subsequent binding of fluorescently labeled SA was detected on the TFT photosensor surface. Approximately, 100 of the TFT elemental devices were used to observe one spot. The signal was converted to an electric current, amplified, and digitized for 2D imaging. Fig. 11.8b shows a TFT photosensor image of the oligonucleotide-array after target DNA was exposed to various concentrations of immobilized oligonucleotide. Initially, biotinylated target DNA for ALDH2*1 was hybridized, and then AlexaFluor-SA was reacted with the biotin-labeled DNA on the surface of the photosensor. Fluorescent spots were observed only on the ALDH2*1 detection oligonucleotide-arrayed photosensor and *not* on the ALDH2*2 detection oligonucleotide-arrayed photosensor (Fig. 11.8b). The use of the TFT photosensor will allow the development of a disposable photodetecting device for DNA chip systems.

11.4 Conclusions

In this chapter, the role of electrochemical and magnetic biosensors towards development of portable, compact and inexpensive biochip devices has been demonstrated. Direct measurement of electrochemical signals, such as ferrocene molecule, is a preferred approach to simplify the process towards miniaturized biochip devices. Furthermore, the use of magnetic probes promises to increase the sensitivity. Future research may be in the direction of developing new probes, e.g. nanomaterials for differing bio-applications.

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