Improvement of insertion loss and quality factor of flexural plate-wave-based alpha-fetoprotein biosensor using groove-type reflective grating structures

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Abstract. Conventional flexural plate-wave (FPW) transducers have limited applications in biomedical sensing due to their disadvantages such as high insertion loss and low quality factor. To overcome these shortcomings, we propose a FPW transducer on a low phase velocity insulator membrane (5-μm-thick SiO₂) with a novel groove-type reflective grating structure design. Additionally, a cystamine self-assembly monolayer and a glutaraldehyde cross-linking layer are implemented on the backside of the FPW device to immobilize alpha-fetoprotein (AFP) antibody. A FPW-based AFP biosensor with low detection limit (5 ng/mL) can be achieved and used to measure the extreme low concentration of AFP antigen in human serum for early detection of hepatocellular carcinoma. The proposed FPW-based AFP biosensor also demonstrates a very high quality factor (206), low insertion loss (−40.854 dB), low operating frequency (6.388 MHz), and high sensing linearity (90.7%). © The Authors. Published by SPIE under a Creative Commons Attribution 3.0 Unported License. Distribution or reproduction in any form, electronic or mechanical, including reuse in other journals or books, is allowed provided that the articles are clearly marked as being from this journal and the first article is cited with an DOI number: 10.1117/1.JMiME.12.1.013017

Subject terms: flexural plate-wave; insertion loss; quality factor; groove-type reflective gratings; self-assembly monolayer; alpha-fetoprotein biosensor.

Paper 12131 received Dec. 17, 2012; revised manuscript received Feb. 24, 2013; accepted for publication Mar. 1, 2013; published online Mar. 20, 2013.

1 Introduction

Over the past few decades, many tumor markers have been proposed as important indicators to screen cancer patients in clinical applications. For instance, discovered by Bergstrand and Czar, alpha-fetoprotein (AFP) is one among the important tumor markers produced by embryonic hepatic cells and the yolk sac. Typically, the serum AFP level in a healthy adult is lower than 20 ng/mL. The high concentrations of AFP in adult have been discovered in hepatocellular carcinoma (HCC) and malignant germ cell tumors of the ovary and testis. In Taiwan and other Asian countries, AFP is commonly used as a tumor marker to screen HCC.

Although the conventional immunoassay methods such as radioimmunoassay and non-isotopic immunoassays [e.g., enzyme-linked immunosorbent assay (ELISA)] both have the advantages of very low detection limit (<10 ng/mL) and accuracy (>90%), they are time-consuming and require skilled personnel to operate in a laboratory. Recently, due to an increasing need for rapid immunoassay test kits for clinical applications, many miniaturized immunosensors with high mass-sensitivities have been developed by various physical transducers to reduce the response time, testing cost, and skilled operation requirement. Combined with the essential specificity of antigen-antibody reactions, some of these immunosensors have gained attention as methods for clinical diagnosis.

In general, the performance of an immunosensor is measured by its capability to detect molecular layers deposited on a surface. For instance, the loading mass on the sensing surface of conventional acoustic sensors can affect some propagating properties of the acoustic wave. Among the acoustic sensors, Lamb waves-based acoustic sensors are frequently used because of their high sensitivity to mass-loading. One of these Lamb modes, the zero order anti-symmetrical mode (A₀), also called flexural plate-wave (FPW), is very suitable for biosensing applications because it has low phase velocity and small radiation loss when propagated in the testing liquid. FPW-based acoustic biosensors have many clinical, industrial, environmental, and biological sensing applications as they demonstrate high sensitivity and accuracy, short response time, low cost, and operating frequency. Any small changes in the mass of floating thin plate of the FPW transducer resulting in a change of the acoustic wave velocity can be measured indirectly as a change in center frequency of the FPW-based biosensor. However, the high insertion loss and low quality factor of conventional FPW-based biosensors have limited their applications. To enhance the quality factor and reduce the insertion loss and phase velocity of a FPW-based biosensor, this paper introduces a novel groove-type reflective grating structure (RGS) and adopts a low phase velocity insulator membrane (5-μm-thick SiO₂) to replace the conventional silicon-based membrane.

The highly specific AFP antigen-antibody interaction is a good candidate for the AFP molecular recognition process. To ensure the AFP molecular with no-specific binding of other bio-molecules, an appropriate self-assembled monolayer (SAMs) must be developed. The use of SAMs in various fields of research is growing rapidly. SAMs have been particularly applied in many biomedical fields as an interface layer between the gold electrode surface and testing solution to enhance the specific antigen-antibody interaction during the molecular recognition process.
In this study, we propose well-bonded cystamine-SAM/glutaraldehyde cross-linking layers for the immobilization of the AFP antibody. A conventional ELISA reader was used to quantitatively analyze the optical density (OD) value of the absorbed AFP antibody/antigen pairs. A commercial finite element software ANSYS was adopted to estimate the phase velocity and the mass-sensitivity of the presented FPW device. The insertion loss, operating frequency, and quality factor of the FPW transducer were investigated by a commercial network analyzer. Utilizing micro-electromechanical systems (MEMS) and cystamine-based SAM technologies, this study demonstrates a FPW-based biosensor with low insertion loss, low operating frequency, high quality factor, and sensing linearity for detecting low concentration of AFP antigen in human serum.

2 Theory Description, Simulation, and Design

2.1 Theory Description

In a FPW device, the acoustic wave propagates in a very thin plate whose thickness is much less than the wavelength. The acoustic energy is present on both sides of the plate, so the entire plate undergoes mechanical deformation. As the ratio of plate thickness to wavelength is very small, the phase velocity of the device is lower than that of most liquids, which results in no radiation from the plate to testing liquid. On the other hand, due to the low phase velocity, the operating frequency of the FPW device for a given wavelength is low, since

\[ f_0 = \frac{V_p}{\lambda}, \]

where \( \lambda \) represents the acoustic wavelength and \( V_p \) is the phase velocity of the FPW. The mass-loading of the Si\(_3\)N\(_4\)/SiO\(_2\)/ZnO/Au floating thin plate which causes changes in operating frequency is given by the following equation:

\[ \frac{\Delta f}{f_0} = S_m \Delta m, \]

where \( \Delta f \) denotes the change of the operating frequency due to a change in mass per unit area (\( \Delta m \)) and \( S_m \) is the mass-sensitivity of the FPW device.

2.2 Propagation Properties Modeling of FPW

Based on the proposed FPW theory, the propagation phase velocity of FPW will be affected by the thickness of thin floating plate. In this paper, a relatively simple model of two different thin floating plates (Si\(_3\)N\(_4\)/Si/Au/ZnO and Si\(_3\)N\(_4\)/SiO\(_2\)/Au/ZnO) has been established to investigate the influence of thickness and material of plate substrate on the phase velocity of FPW. Conventional FPW devices are constructed by Si\(_3\)N\(_4\)/Si/Au/ZnO multilayer and their phase velocities are about 900 to 1000 m/s. To reduce the phase velocity and operating frequency of FPW, this work replaces the silicon thin plate material by silicon dioxide. The finite element model of the proposed thin floating plates is shown in Fig. 1(a). The length of the plate and the thickness of Si\(_3\)N\(_4\)/Au/ZnO multilayer are set at 100 and 0.15 μm/0.15 μm/1 μm, respectively. Since the thickness of chromium (0.02 μm) is much less than that of gold electrode, it can be neglected in our simulation. The thickness of Si or SiO\(_2\) was varied from 1 to 10 μm during the phase velocity simulation by commercial finite element software (ANSYS). All physical properties of materials adopted in this research are listed in Table 1. This simulation used two-dimensional solid structure elements that model plane strain condition in the Z direction. These elements are defined by four nodes with 2 deg of freedom. In order to obtain the Lamb wave modes, each pair of symmetric nodes from the two ends of the model was coupled. The eigenvalue problem was solved using Lanczos algorithm.

![Diagram](https://example.com/diagram.png)

**Fig. 1** (a) A simple finite element model of the proposed Si\(_3\)N\(_4\)/SiO\(_2\)/ZnO/Au thin floating plate. (b) Simulated mode shape of flexural plate-wave.

<table>
<thead>
<tr>
<th>Material properties</th>
<th>Si</th>
<th>ZnO</th>
<th>SiO(_2)</th>
<th>Au</th>
<th>Si(_3)N(_4)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Young’s modulus E(GPa)</td>
<td>190</td>
<td>1</td>
<td>70</td>
<td>78</td>
<td>300</td>
</tr>
<tr>
<td>Density ρ/(kg/m(^3))</td>
<td>2330</td>
<td>5665</td>
<td>2200</td>
<td>19300</td>
<td>3100</td>
</tr>
<tr>
<td>Poisson ratio ν</td>
<td>0.23</td>
<td>—</td>
<td>0.2</td>
<td>0.44</td>
<td>0.27</td>
</tr>
</tbody>
</table>

\[^{[C]}\] represents the stiffness matrix of the ZnO adopted in this research.

\[
[C] = \begin{bmatrix}
20.97 & 12.11 & 10.51 & 0 & 0 & 0 \\
12.11 & 20.97 & 10.51 & 0 & 0 & 0 \\
10.51 & 10.51 & 21.09 & 0 & 0 & 0 \\
0 & 0 & 0 & 4.43 & 0 & 0 \\
0 & 0 & 0 & 0 & 4.21 & 0 \\
0 & 0 & 0 & 0 & 0 & 4.24
\end{bmatrix} \times 10^{10} \text{N/m}^2
\]
Table 2 Simulated eigenfrequencies of FPW thin floating plate with different Si ($F_1$) and SiO$_2$ ($F_2$) thicknesses.

<table>
<thead>
<tr>
<th>Thickness (μm)</th>
<th>$F_1$ (MHz)</th>
<th>$F_2$ (MHz)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>2.43</td>
<td>2.219</td>
</tr>
<tr>
<td>2</td>
<td>3.76</td>
<td>3.314</td>
</tr>
<tr>
<td>3</td>
<td>5.16</td>
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<td>9</td>
<td>13.642</td>
<td>10.169</td>
</tr>
<tr>
<td>10</td>
<td>14.968</td>
<td>11.023</td>
</tr>
</tbody>
</table>

Fig. 2 Simulated phase velocity of the proposed FPW device with ten different thicknesses of Si and SiO$_2$ thin layer.

for an upper frequency band of 20 MHz. This algorithm can find out all the mode shapes in the given frequency range. With these restrictions, the mode shape of the simulated $A_0$ mode of the Lamb wave (which also called FPW) can be obtained from a modal analysis as shown in Fig. 1(b). All the simulated eigenfrequencies with different thickness of Si and SiO$_2$ are shown in Table 2. It is noticeable that the length of plate shown in Fig. 1(b) is equal to one complete FPW wavelength, so the phase velocity can be calculated directly by Eq. (1) and the results are shown in Fig. 2. Obviously, the phase velocity of FPW propagated in SiO$_2$ is much slower than in Si under the same thickness. Consequently, in addition to low operating frequency, the operating frequency of SiO$_2$-based FPW is less sensitive to the thickness of thin plate and therefore it is very suitable for the development of a high stability FPW sensor. Furthermore, to analyze the mass-sensitivity of the proposed FPW device, this study simulated five different gold thicknesses (50 to 250 nm) deposited on the backside of a 0.15 μm Si$_3$N$_4$/5 μm SiO$_2$/0.15 μm Au/1 μm ZnO thin floating plate. The simulated frequency shifts under the different thicknesses of backside gold layer are shown in Fig. 3. The calculated phase velocity and mass-sensitivity of the proposed FPW device are equal to 643.7 m/s and 112 cm$^2$/g, respectively.

2.3 Reflective Coefficient of the Proposed Groove-Type RGS

The interdigital transducer (IDT) structure is a bidirectional device and it can be converted into a unidirectional device by properly utilizing a reflector as proposed by Zaitev and Joshi. In this paper, we adopted groove-type RGS as the reflector of FPW and the depth of each SiO$_2$-groove was 1.5 μm. Nakagawa and his co-worker have presented a quantitative estimate equation of the reflection coefficient ($R$) of a Lamb wave with a grating reflector as shown in the following equation:

$$ R = \tan h(\gamma) = \tan h\left(\frac{2\rho_m V_{pm} - \rho_f V_{pf}}{\rho_m V_{pm} + \rho_f V_{pf}}\right). $$

Fig. 3 Simulated frequency shifts of the proposed FPW device under five different thicknesses of backside gold layer.

Here, $\rho_m$ and $\rho_f$ are the equivalent mass densities of Si$_3$N$_4$/SiO$_2$/Cr/Au/ZnO floating thin plate with and without groove-type RGS, which can be calculated as 2237 and 3178.5 kg m$^{-3}$, respectively. The $V_{pm}$ and $V_{pf}$ represent the phase velocity of lamb wave propagated in the Si$_3$N$_4$/SiO$_2$/Cr/Au/ZnO floating thin plate with and without groove-type RGS; their simulated values are equal to 429.4 and 643.7 m/s, respectively. Finally, based on Eq. (3), a 61.82% reflection coefficient of the 1.5-μm-depth groove-type RGS can be obtained.

2.4 Layout Specification of the Proposed FPW Device

Figure 4 shows a layout diagram of the designed FPW device with groove-type RGS using commercial AutoCAD software. The major design parameters of the designed FPW devices are listed in Table 3. As the width and gap of the IDT finger electrodes are 25 μm, the theoretical wavelength of FPW generated from these IDTs is equal to 100 μm (four times of IDT finger width). Both input and output IDTs of
the FPW device are constructed by 25 pairs of Cr/Au fingers. The acoustic aperture and path length of the FPW device are 2 and 1.5 mm, respectively. Each RGS of the FPW device is constructed by 3 pairs of etched grooves. The separation gap between adjacent transducer fingers plays essentially no role in transduction. It is widely accepted that the (111) plane of the gold (Au) metal layers can match well with the (002) plane of ZnO layer. A 200-A-thick Cr and a 1500-A-thick Au were continually deposited onto Si/SiO 2 /Si 3 N 4 /SiO 2 layers by an e-beam evaporator to form a ground plane of the FPW device. The Au and Cr thin layers were patterned by the Au etchant (3% I 2 : 40% KI: 57%H 2 O) and the Cr etchant (Cr-7T), respectively.

Since the last decade, many piezoelectric thin films have been developed for the application of acoustic micro sensors. Three most popular piezoelectric thin-film materials are the ZnO, AlN, and PZT. In this study, a high quality C-axis orientation ZnO piezoelectric layer was deposited on the Cr/Au ground plane by RF magnetron sputter and patterned by wet etching method (3%H 3 PO 4 : 3%CH 3 COOH: 94H 2 O). The major advantages of magnetron sputtering are that the electron bombardment of the substrate can be greatly reduced and the temperature of substrate can be better controlled by an external heater. A 200-A-thick Cr and a 1500-A-thick Au layer was deposited by an e-beam evaporator and patterned by lift-off photolithographic method to construct the IDTs. To implement the FPW transducer with 1.5-μm-depth groove RGS, additional photolithograph and silicon etching (by reactive ion etching systems) processes must be adopted, as shown in Fig. 6. The backside Si was etched in 30 wt%, 80°C KOH anisotropic etching solution for approximately 7 h until the whole silicon material in the backside cavity was removed. Therefore, a 0.15 μm Si 3 N 4 /5 μm SiO 2 /0.02 μm Cr/0.15 μm Au/1 μm ZnO floating thin plate of the proposed FPW device can be obtained. Finally, a 0.02-μm-thick Cr and a 0.15-μm-thick Au were continually deposited on to the backside cavity for SAM immobilization.

### 3 Experiment

#### 3.1 Fabrication of the FPW Device

The main processing steps of the presented SiO 2 -based FPW device are shown in Fig. 3. The 5000-A-thick silicon dioxide and the 1500-A-thick silicon-rich low-stress nitride were grown and deposited on a 530-μm-thick 4-inch (100) silicon wafer by thermal furnace and low-pressure chemical vapor deposition system. A 5-μm-thick silicon dioxide was then deposited onto the top side by plasma enhanced chemical vapor deposition system to be the supported film for yield improvement and life time enhancement. The backside Si 3 N 4 was patterned by reactive ion etching system for further backside silicon etching. As the proposed FPW devices have a conducting ground plane opposite and close to the IDTs, the transverse electric fields set up by the voltages between adjacent transducer fingers plays essentially no role in transduction. It is widely accepted that the (111) plane of the gold (Au) metal layers can match well with the (002) plane of ZnO layer. A 200-A-thick Cr and a 1500-A-thick Au were continually deposited onto Si/SiO 2 /Si 3 N 4 /SiO 2 layers by an e-beam evaporator to form a ground plane of the FPW device. The Au and Cr thin layers were patterned by the Au etchant (3% I 2 : 40% KI: 57%H 2 O) and the Cr etchant (Cr-7T), respectively.

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#### 3.2 Immobilization of the Cystamine SAM/ Glutaraldehyde Layers in the Backside Cavity of FPW Device

Molecular self-assembly is the spontaneous organization of molecules into stable, structurally well-defined aggregates. The basic principles of molecular self-assembly are found in the biology; protein folding and aggregation and pairing of base pairs in DNA are two well-known examples. SAMs were preceded historically by Langmuir–Blodgett (LB) monolayers, which have been studied extensively and are useful for many applications. LB films, however, are neither convenient to prepare nor sufficiently robust for most applications. SAMs, in contrast, are more robust and simpler to generate and can be formed from a wide variety of ligands and supports. In this work, the cystamine material with amine-group bonds is adopted as a well self-assembly monolayer between the sensing gold layer and the AFP antibody layer. The detailed immobilization processes of the cystamine SAM on the FPW device are described as follows.

Before the immobilization of cystamine SAM layer, the backside gold layer surface of FPW device was pretreated with the "piranha" solution (70 wt%H 2 SO 4 : 30 wt% H 2 O 2 ) for 30 min to create a hydrophilic surface and improve the adsorption of cystamine SAM molecules and then washed with de-ionized (DI) water three times and dried at room temperature. To immobilize the SAM layer onto the gold
layer, the chip was immersed in a cystamine solution (0.02 M) for 1 h and washed with DI water three times and air-dried. The chips were further dipped into 1.25 wt % aqueous glutaraldehyde cross-linking reagent for 1 h incubation process and washed with DI water three times.

### 3.3 Dip Coating of the AFP Antibody/BSA/AFP Antigen in the Backside Cavity

After the highly purified mouse anti-human AFP antibody layer coated on the surface of the backside glutaraldehyde layer, a diluted bovine serum (BSA) layer was used for blocking and incubating the AFP antibody-coated surface to avoid non-specific absorption. The final configuration of the FPW-based biosensor and the integrated cystamine SAM/glutaraldehyde/AFP antibody/AFP antigen multilayer are schematically displayed in Fig. 6(a) and 6(b), respectively. The detailed procedures are described as follows:

1. Washed by 1 c.c. phosphate buffered saline solution three times.
2. Dip 10 μL diluted rabbit AFP antibody (27°C, 2 h).
3. Inject 200 μL Tween-20 wash buffer three times.
4. Inject 10 μL, 1 wt% BSA solution (27°C, 0.5 h).
5. Inject 200 μL Tween-20 wash buffer three times.
6. Inject 10 μL diluted human AFP antigen (27°C, 2 h).
4 Results and Discussion

4.1 Quantification Analysis of the AFP
Antibody-Antigen Immobilized on 96-Well
Micro-Titer Plate and Si/SiO₂/Si₃N₄/Cr/Au/
Cystamine/Glutaraldehyde Chip

Solid-phase assays for antibody employing ligands labeled
with radioisotopes or enzymes (ELISA) are probably the
most widely used of all immunological assays because
many samples can be performed in a relatively short
time. In our study, a commercial ELISA was used to quan-
titatively analyze the total AFP concentration in a micro-
titer plate and a high-linearity (99.63%) standard OD
curve were extracted for six concentrations of human
AFP antigen under the same monochromatic light wave-
length (450 nm). A standard OD curve of the AFP antigen
concentration immobilized on a Si/SiO₂/Si₃N₄/Cr/Au/
cystamine/glutaraldehyde/AFP antibody chip (denoted
as SAM/AFP Ab-Ag chip) with the size of 4 mm × 4 mm ×
0.53 mm is also investigated. As shown in Fig. 7, the mea-
sured standard OD curve of the SAM/AFP Ab-Ag chip
presents a very high linearity (99.51%), and thus, demon-
strates the immobilization processes established on the
silicon substrate is reliable for further developments on
the FPW-based biosensor.

4.2 Characterization of the Proposed FPW-AFP
Biosensor

As depicted in Fig. 8(a) and 8(b), the top-view and cross-
sectional SEM of the RF sputtering deposited ZnO layer
reveal its dense, uniform, and columnar grain structures.
The RF sputtering deposited ZnO layer has an average
grain size of about 145 nm and almost without any void.
According to our previous experiences, a ZnO thin film
with apparent columnar grain structures usually presents a
higher C-axis (002) orientation crystallization and coupling
piezoelectric coefficient. Figure 8(c) shows the top-view
SEM of the patterned Cr/Au IDTs and groove-type RGS
of the proposed FPW device. Each RGS of the FPW device
is constructed by 3 pairs of SiO₂ etched grooves with the
depth and width of 1.5 and 25 μm, respectively. The sepa-
ration gap between the RGS and IDTs is 37.5 μm.

The center frequency of the developed FPW device was
measured by the Cascade RHM-06/V probe station and the
Agilent E5074 network analyzer. Two Cascade ACP40-
W coplanar 150 GSG probes were used to contact the
input and output IDTs of the fabricated SAW device and
all the measurements were carried out at room temperature.
As Fig. 9(a) shows, the measured center frequency of the
implemented FPW device is 6.388 MHz, which agrees
well with the simulated result (6.437 MHz). Figure 9(b)
shows the frequency response measured after 0.02 μm
Cr/0.15 μm Au thin films are deposited on the bottom of
backside cavity of the FPW device. Obviously, as the backside
Cr/Au thin films are deposited, the Q value of the original
FPW device (206) is decreased to 148 and the center fre-
quency of FPW shifted from 6.388 to 6.221 MHz due to

Fig. 7 The AFP standard OD curves of the 96-well microtiter plate
and the Si/SiO₂/Si₃N₄/Cr/Au/cystamine/glutaraldehyde chip
extracted by ELISA.

Fig. 8 (a) Top view and (b) cross-sectional SEM images of the RF
sputtering deposited ZnO thin film. (c) The top-view SEM of the pat-
terned Cr/Au IDTs and groove-type RGS of the presented SiO₂-
based FPW transducer.

J. Micro/Nanolith. MEMS MOEMS
013017-6 Jan–Mar 2013/Vol. 12(1)
the mass-loading effect. According to the theory described in Secs. 2 to 3, as the backside Cr/Au thin films are deposited, the equivalent mass densities of Cr/Au/Si₃N₄/SiO₂/Cr/Au/ZnO floating thin plate with and without groove-type RGS can be increased from 2237 to 2910.5 kg m⁻³ and increased from 3178.5 to 3553.5 kg m⁻³, respectively. The simulated phase velocity of the Lamb wave propagated in the Cr/Au/Si₃N₄/SiO₂/Cr/Au/ZnO floating thin plate with and without groove-type RGS is equal to 383.6 and 621 m/s, respectively, which is smaller than that of Si₃N₄/SiO₂/Cr/Au/ZnO floating thin plate (429.4 and 643.7 m/s). Based on Eq. (3), the reflection coefficient of the 1.5-μm-depth groove-type RGS in a Cr/Au/Si₃N₄/SiO₂/Cr/Au/ZnO floating thin plate is 57.5%, which is smaller than that of in the Si₃N₄/SiO₂/Cr/Au/ZnO floating thin plate (61.82%). It can be concluded that as 0.02-μm-thick Cr and 0.15-μm-thick Au thin films are deposited on the backside cavity, the reflection coefficient of groove-type RGS is decreased and results in a reduced Q value of FPW device.

Compared to our previous research, the proposed FPW device has demonstrated a lower insertion loss (−40.854 dB), lower operating frequency (6.388 MHz), and higher quality factor (206) than conventional FPW devices with Si-based thin plate and without RGS design. Calculated by Eq. (4), the mass-sensitivity of the proposed FPW sensor is equal to 86.03 cm²/g. Finally, this research measured the center frequency shift under six various concentrations of the AFP antigen coated to the backside cavity of FPW-based AFP biosensor and each testing condition is measured three times. As Fig. 10 shows, the proposed FPW-based AFP biosensor can demonstrate a very low detection limit of AFP antigen (5 ng/mL) and a high sensing linearity (90.7%).

### 5 Conclusion

In this paper, a groove-type RGS design has been adopted to improve the insertion loss and quality factor of conventional FPW-based biosensors. According to the finite element analysis results, this work also replaced silicon with silicon dioxide as the main material of FPW thin plate to reduce the operating frequency and sensitivity to thickness variation. The simulated phase velocity of the proposed FPW device constructed by Si₃N₄/SiO₂/ZnO/Cr/Au multilayer is equal to 643.7 m/s, much less than that of acoustic wave in most of testing liquid. The measured center frequency of the implemented FPW device is only 6.388 MHz, which agrees well with the simulated result (6.437 MHz) and thus can facilitate the development of readout integrated circuits. Additionally, the mass-sensitivity of proposed FPW sensor reaches 86.03 cm²/g and approximates the simulated results (112 cm²/g). By utilizing MEMS and cystamine-based SAM technologies, a novel FPW-AFP biosensor can demonstrate a very low detection limit of AFP antigen (5 ng/mL) and a high sensing linearity (90.7%).

### Acknowledgments

The authors would like to thank the National Science Council and National Sun Yat-sen University of the
Republic of China, Taiwan, for financially supporting this research under Contract Nos. NSC 100-2221-E-110-021, NSC 101-2221-E-110-080, and 111-28-05-101. The authors are indebted to the National Nano Device Laboratories in Taiwan for their assistance in providing access to their processing facilities. The authors also thank Dr. B. S. Hsieh of Kaohsiung Medical University for her technical support in ELISA tests.

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