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A Low-cost Biomarker-based SAW-Biosensor Design for Early Detection of Prostate Cancer

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Abstract

Early detection of prostate cancer is crucial for the treatment. Currently rectal examination, ultrasound and ELISA test for blood-PSA biomarker level are used for diagnosis. However these methods require professional assistance that makes point-of care (POC) testing impossible. A POC, low-cost, high-precision biosensor can increase the early-detection and survival rates. Recently, we have proposed a low-cost and an easy-to-use surface acoustic wave biosensor that enables the quantification of PSA level. In this study, we focused to the electronic circuitry and signal processing algorithms for accurate protein level assessment using cost efficient and low-profile hardware. Simplifying the hardware will potentially lead to the development of single chip monolithic integrated biosensor.

The MEMS based biosensor designed in our studies utilizes shear-horizontal (SH) SAWs on ST-cut Quartz substrate to sense the mass loading change by protein adhesion. The driver circuitry employs signal-processing algorithms to detect the phase change, which quantifies the protein level in the sample dropped on the surface.

The signal applied to the sensor input is a 16.9 MHz square wave generated by using a simple counter circuit. The output is under-sampled at an extremely low rate (100 KHz), then, the phase information is extracted using the under-sampled signal. A low-profile microcontroller (μC) is used to determine the phase shift. The simulated and experimental results are demonstrated, and they agreed well with each other. The results show that, the phase error level is 1% and minimum delay measured is 0.3 ns. Increasing number of samples used for calculation enhances the detection performance. Our studies also showed that using excessive number of samples enables the accurate phase calculation even if a simple 1-bit ADC is employed.

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Keywords: Biosensor; Surface acoustic wave; acurate phase detection; MEMS

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Prostate cancer is the second leading cause of death according to the statistics, however, early diagnosis increases patients' recovery rate [1]. Prostate-specific antigen (PSA) has provided convenience in diagnosis and staging of prostate cancer, and follow-up of patients. Today, the tests to measure the PSA level are done using Enzyme Linked Immunosorbant Assay (ELISA) method. However, this method can be applied only in hospitals or clinical laboratories. Furthermore, free-PSA is an unstable molecule at room temperature and 4 ° C, it leads to difficulties in the storage and evaluation. In contrast, a biosensor-based method, which enables to analyze the sample quickly, will increase the accuracy of the results. Recently we have proposed a low-cost and an east-to-use surface acoustic wave biosensor that enables the quantification of PSA level [2]. In this study, we focused to the electronic circuitry and signal processing algorithms for accurate protein level assessment using low-cost, low-profile hardware.

SAW based biosensors can measure the protein level in the dropped sample by measuring amount of delay induced to the input signal. Hence, phase change can quantify the protein level in the sample. The SAW biosensors have quite narrow-band and high-frequency characteristics, therefore utilized high frequency electronics increase the complexity and the costs of the reader electronics. In the literature, there are several methods developed to down-sample the narrow band signals with no information loss (like band-pass sampling) [3]. Furthermore, In our study, the down-sampling does not corrupt the phase information as shown in equations (1)-(3), where $s(t)$, $s_{ADC}(t)$ and $s_D(t)$ are the output, sampled and down-sampled signals respectively. φ represents the input/output phase difference, f_0 denotes SAW frequency, T_{ADC} is the sampling period and N_D is decimation factor. The phase difference can be accurately determined using only the s_D signal by using a simple FFT algorithm.

$$s(t) = \sin(2\pi f_0 t + \varphi) \quad (1), \quad s_{ADC}(t) = \sin(2\pi T_{ADC} n + \varphi) \quad (2), \quad s_D(t) = \sin(2\pi T_{ADC} N_D k + \varphi) \quad (3).$$

We tested our method using simulations and the experiments, which are agreed well when a reasonable noise signal (18%) is added to the simulations. The parameters and experimental setup can be seen in Fig. 1 and Table 1. The results for 4500 samples show that the average errors are 0.04° and 0.06°, the deviations are 0.15 ° and 0.18 ° for the experiment and simulation results respectively. Mean error is increasing to 0.2° if the used number of samples is decreased to 500. Simulations show that the error and the deviation is close to zero if number of samples is 50000. The experiments and the simulations are repeated for the different phase angles. It showed that, the phase error is independent from the phase angle. The effect of number of bits (ADC) on the phase error is measured through experiments and simulations. It is presented that number of bits (ADC) can be decreased without compromising the phase error if number of samples is high enough. The phase error is 0.18 ° when 4500 samples and 1-bit ADC are used. Simulation studies show that, if 50000 samples are used, the phase error is close to zero for 1-bit ADC setup.

In this study a low-cost and simple driver circuit is designed and tested for a biosensor. Decreased complexity makes the monolithic IC-sensor integration possible. The test results show that the simplified driver circuit provides remarkable measurement performance.

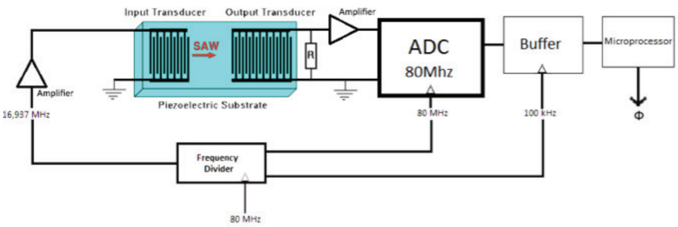

Fig. 1.Experiment setup

Table 1. Experiment and simulation parameters.

Parameters	Experiment	Simulation
Number of samples	500,4500	500-50000
Numb. of bits of ADC	1-3-5-7-9-10	1-3-5-7-9-10
ADC frequency	80MHz	80 MHz
Decimation ratio	799	799

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References

[1] Howlader N, Noone AM,. et al. ,SEER Cancer Statistics Review, Natioanl Cancer Institute,1975-2013.
[2] Onen, O.; Sisman, A., et al., A Urinary Bcl-2 Surface Acoustic Wave Biosensor for Early Ovarian Cancer Detection, Sensors, 2012.
[3] R. G. Vaughan, et al., The Theory of Bandpass Sampling, IEEE Trans. On Signal Proc., 1991