A Novel Frequency-shift Readout System for CEA Concentration Detection Application

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Abstract—**This paper demonstrates a novel frequency-shift readout system for CEA (carcinoembryonic antigen) concentration detection. The proposed system comprises a scanning signal generator, a power detector, and a control circuit. Since the frequency-shift range of FPW (flexural plate wave) sensors is around 1 ~ 20 MHz, the proposed power detector contains an amplitude to voltage convertor to carry out the required sensing function. The proposed system doesn't need any high bandwidth OPAs. The measurement results based on FPGA verification show that the linearity of the proposed system is 0.983, where the maximum output error is 0.15 MHz.**

Keywords—Analog processing circuit, resonant frequency, power detector, peak detector, frequency-shift readout circuit

I. Introduction

According to the statistical data published by the WHO in 2014, there are approximately 14 million new cases and 82 million deaths related to cancer in 2012. The 5 most common slides of cancer diagnosed in 2012 were lung, livers, stomach, colorectal, and breast. In order to cure and discover cancers at very early stage, the CEA blood test has recently been widely used. Notably, CEA is mainly used as a tumor marker for cancers of lung, livers, stomach, colorectal, and breast, etc [1] – [3]. Most of the healthy people, even the smoking ones, the CEA concentration in blood should be lower than 5 ng/mL. If a person whose CEA concentration in blood is higher than 10 ng/mL, he or she may have high stake of various cancers.

Currently, the ELISA (enzyme-linked immunosorbent assay) and QCM (quartz crystal microbalance) have long been used to measure the CEA concentration [4]. However, the ELISA or QCM is not suitable for the clinics in the remote and suburban areas because of long operating time and high cost. To resolve the problems, based on the fact that the resonant frequency-shift of the FPW sensor is proportional to the CEA concentration, Liao *et al.* reported a CEA concentration measurement system in 2013 [5]. However, Liao's readout system has two problems.

1. OPA with high bandwidth input range: Since the resonant frequency-shift range of the FPW sensor is about 1 ~ 20 MHz, Liao's system needs two high bandwidth OPAs, where one follows with the sensor and the other is used to be an unit gain buffer in the peak detector.
2. Too many OPAs in the peak detector: In Liao's peak detector, the filter stage is required to filter out high-frequency components of the sensor output, where at least two OPAs are needed.

This paper presents a novel frequency-shift readout system. The high input bandwidth requirement has been relaxed by an amplitude to voltage convertor (AVC). Since the AVC will generate a DC voltage proportional to the input amplitude, the filter stage is no longer needed. The proposed readout system will be introduced in the next section and the measurement result is given in Section IV.

II. Circuit Design and Analysis

Fig. 1 shows the architecture of the proposed frequency-shift readout system. The proposed frequency-shift readout system contains three parts: scanning signal generator, power detector, and control circuit. The frequency of the scanning signal, which is generated by the scanning signal generator, increases with the time (namely, counter). Since the sensor has different frequency response at different input frequency, the amplitude of the $V_{in}(t)$, sensor's output, will vary along with the scanning signal frequency. The AVC in the power detector filters out the AC components and generates a DC voltage. After the gain stage enlarges the AVC output, the peak detector detects the maximum input voltage and sends a flag signal to the control circuit. Finally, the control circuit will calculate the CEA concentration by the resonant frequency difference between before and after the standard test solutions which is titrated into the FPW sensor. Because the scanning signal generator is our previous work reported in 2011 [6], there is no need to rephrase hereby. The details of the power detector will be introduced in following text.

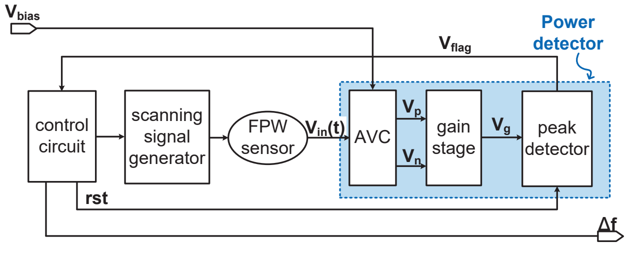

Fig. 1. The architecture of the proposed frequency-shift readout system.

III. Power Detector in the Proposed System

The proposed power detector is composed of an AVC, a gain stage and a peak detector. Fig. 2 shows the proposed AVC, which is used to convert input amplitude into a proportional DC voltage. Since the M_{101} is driven into saturation region by

V_{bias}, and C_{101} blocks the input DC term, the current of M_{101} is shown as follows.

$$i_{M_{101}}(t) = \frac{1}{2} \cdot \beta_n \cdot (V_{in}(t) + V_{bias} - V_{TN})^2 \quad (1)$$

where $\beta_n = \mu_n C_{ox}(W_{101}/L_{101})$ is the MOSFET transconductance parameter. The C_{102} and C_{103} are utilized to ground out the AC terms of the output voltages. Therefore, the differential output voltages is shown as follows.

$$V_{diff} = V_p - V_n = \frac{\beta_n}{2} \cdot R \cdot V_{in}(t)^2 \quad (2)$$

To increase the sensitivity of the proposed frequency-shift detector, the gain stage is required to amplify the AVC output. When the sensor has a maximum output amplitude, which indicates that the frequency of the scanning signal is equal to the resonant frequency of the FPW sensor, the peak detector will send a flag signal to trigger the register in the control circuit to store the scanning signal information. After the standard test solutions is titrated into the FPW sensor, the scanning process will be repeated to calculate the CEA concentration of the solution.

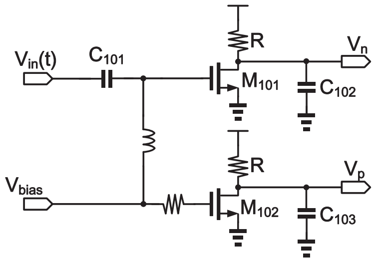

Fig. 2. The schematic of the proposed AVC.

IV. Implementation and Measurement

The proposed frequency-shift readout system is realized using discretes and an FPGA board (including the scanning signal generator and control circuit), as shown in Fig. 3. Fig. 4 shows the measurement results, where the linearity is $R^2 = 0.983$ and the maximum error is 0.15 MHz. The comparison with our previous work is tabulated in Table I. The proposed frequency-shift readout system only needs two OPAs (one is in gain stage, and the other is in the proposed peak detector) such that it effectively reduces the complexity. More importantly, there is no need of any high bandwidth OPAs.

V. Conclusion

This paper presents a novel frequency-shift readout system for CEA concentration detection. The proposed circuit is able to detect the resonant frequency of the FPW sensor with only maximal 0.15 MHz error. By the measurement results, the linearity of the proposed frequency-shift detector is proves to be $R^2 = 0.983$.

Acknowledgment

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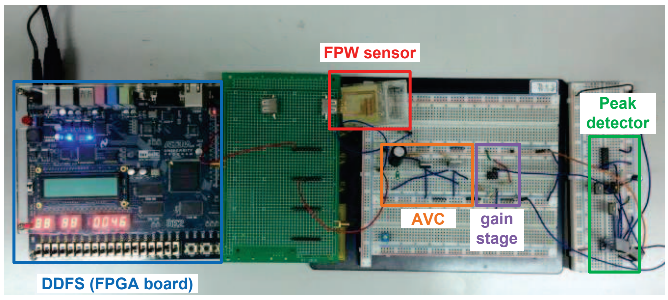

Fig. 3. Photo of the experimental environment.

TABLE I. Comparison with Prior Works

	[5]	[7]	This work
year	2013	2014	2016
technology	FPGA & chip	FPGA & chip	FPGA & discretes
linearity	None	0.9772	0.983
maximal error	None	0.12 MHz	0.15 MHz
number of OPA	4 (at least)	4 (at least)	2

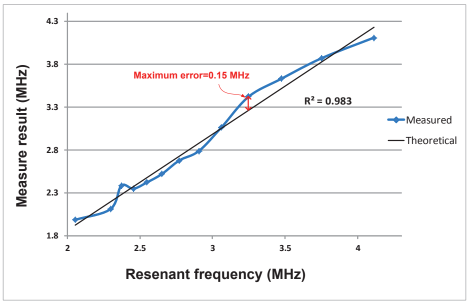

Fig. 4. The measurement results of the proposed system.

References

[1] M. Grunnet and J. B. Sorensen, "Carcinoembryonic antigen (CEA) as tumor marker in lung cancer," *World Journal of Surgery*, vol. 76, no. 2, pp. 138, May 2012.

[2] M. J. Duffy, "Carcinoembryonic antigen as a marker for colorectal cancer, " *Clinical Chemistry*, vol. 47, no. 4, pp. 624-630, Apr. 2001.

[3] D. Pectasides, A. Mylonakis, M. Kostopoulou, M. Papadopoulou, D. Triantafillis, J. Varthalitis, M. Dimitriades, and A. Athanassiou, "CEA, CA 19-9, and CA-50 in monitoring gastric carcinoma," *World Journal of Surgery*, vol. 20, no. 4, pp. 348, Aug. 1997.

[4] I.-Y. Huang, M.-C. Lee, C.-H. Hsu, and C.-C. Wang, "Development of a FPW allergy biosensor for human IgE detection by MEMS and cystamine-based SAM technologies," *Sensors & Actuators B: Chemical*, vol. 132, no. 1, pp. 340-348, May 2008.

[5] C. -C. Wang, T. -C. Sung, C. -H. Liao, C. -M. Chang, J. -W. Lan, and I. -Y. Huang, "A CEA concentration measurement system using FPW biosensors and frequency-shift readout IC," *IEEE Inter. Conf. on Electronics, Circuits and Systems* (ICECS), pp. 27-30, Nov. 2013.

[6] C. -H. Hsu, Y. -C. Chen, and C. -C. Wang, "ROM-less DDFS using non-equal division parabolic polynomial interpolation method," *IEEE Inter. Symposium on Integrated Circuits*, pp. 59.62, Dec. 2011.

[7] C. -C. Wang, C. -H. Liao, C. -M. Chang, J. -W. Lan, and I. -Y. Huang, "A fast CEA analyzer prototype for point of care testing," *IEEE Inter. Conf. on Electron Devices and Solid-State Circuits* (EDSSC), pp. 1-2, Jun. 2014.