WHITE PAPER

Qorvo Biotechnologies Sensor-based Technology Aims to Provide Rapid Reference-lab Quality Tests at the Point-of-Care

Summary

This white paper describes Qorvo Biotechnologies' Bulk Acoustic Wave (BAW) immunosensor detection platform designed for point-of-care applications and describes analytical and functional sensitivity testing on human Thyroid Stimulating Hormone (hTSH) as an example. The Qorvo Biotechnologies' platform is targeted to be central lab matched, with the goal of providing clinicians data that will enable quicker decision making across multiple disease states, such as in cardiac and infectious disease segments, where time to result and high performance are critical factors in the patient care workflow. Designed to accommodate multiple sample types, such as whole blood, serum, plasma, saliva, urine, and stool, in a universal cartridge design, the platform expands the viable test menu across the clinically relevant spectrum. For hTSH in serum, sensitivity of sub 1 pg/mL (0.005 µIU/mL) in true patient samples has been demonstrated, with a dynamic range of three decades, 1-1000 pg/mL. Compared to a traditional colorimetric based approach, this high-sensitivity solution provides a low limit of detection (LOD), while supporting multiplexed capability in a variety of assay formats.

Qorvo Biotechnologies Platform

The Qorvo Biotechnologies platform is designed as a benchtop system with a small footprint design that integrates easily into an emergency room or point-of-care clinic (Fig 1). The disposable cartridge comes in single use pouches with a simple-to-use sample port.

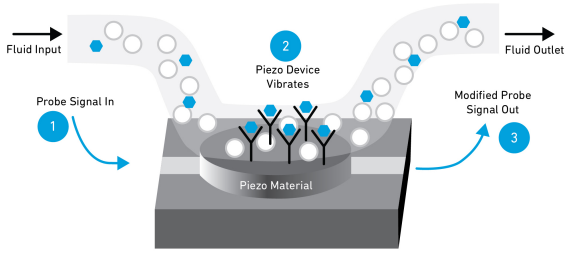
Figure 1. Qorvo Biotechnologies' and Cartridge.

The detection scheme utilizes a gravimetric sensor based on proprietary piezoelectric (BAW) technology, an immunosensor methodology that is well-established in the literature [1-4].

The microfluidics technology integrates traditional biochemistry together with the BAW transducer entirely on the cartridge, allowing for customization of each assay. Using a positive displacement pump, fluid is aspirated from reagent wells on the cartridge and continually moved over the BAW sensor (Figure 2) where the assay reaction occurs.

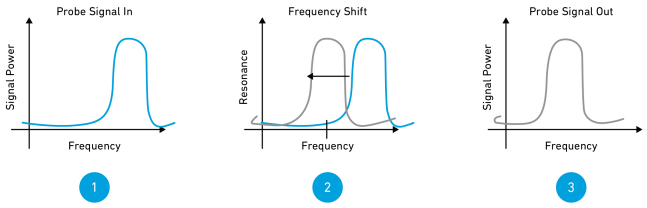
This device is for investigational use only.

Figure 2. (1) RF signal is delivered to a BAW sensor as the fluid moves over the surface, (2) the sensor resonance frequency is modulated as mass is added to the surface and (3) the RF signal is output to the instrument.



As the antigens bind to the device surface, the transducer's native resonance frequency is shifted and dampened due to mass loading (Figure 3). Because the sensitivity of the transducer increases with the square of the frequency, the sensor contrasts with previous immunosensors and conventional fluorescence techniques due to its extremely high sensitivity at its frequency of operation (~ 3 GHz).

Figure 3. (1) Initial frequency reading under fluidic conditions. (2) Mass is added to the surface causing a frequency reduction due to loading. (3) The final output signal can be used to calculate a total frequency shift proportional to the mass binding.

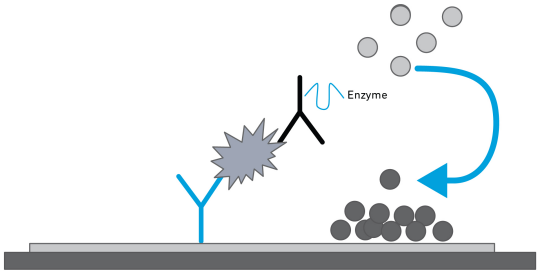


This simple, but sensitive technology, allows for universal biosensors, where the bioactivation of the surface determines the assay. Thus, the universal cartridge design is compatible with immunoassay and potentially molecular detection as well. Additionally, by combining two or more sensors within the fluid path, it is possible to detect a multiplicity of proteins within the same cartridge.

TSH Assay

In the investigative hTSH assay, two sensors are activated on the device surface, one with an Anti-hTSH antibody, and the second with a nonspecific reference antibody; this allows for common mode rejection of spurious signals.

Figure 4. Sandwich immunoassay format with enhancing precipitate (blue spheres).



The sandwich hTSH assay [5] additionally uses an enzymatic enhancement phase, whose insoluble precipitate amplifies the signal (Figure 4). All reagents are held on cartridge and sample preparation is limited to depositing the sample directly into the cartridge. Total time from sample collection to result is under 15 minutes.

Materials and Methods

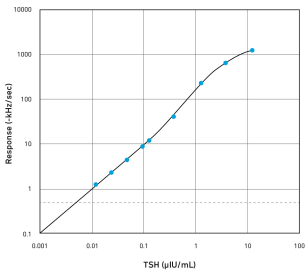
Biological reagents were sourced commercially. The sensor surfaces were activated using a non-contact spotter, and assembled in-house in Plymouth, MN. The serum samples were collected in a clinical setting and tested on the Qorvo Platform (Figure 5) as well as the Roche Cobas e601.

Figure 5. Typical assay workflow.

Results

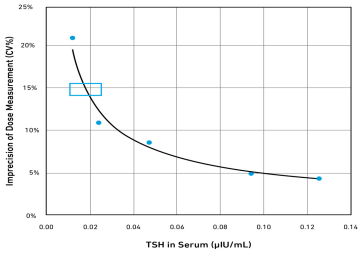
Based on the feasibility testing performed, the hTSH assy has an LOD [6] in human serum of 0.4 pg/mL sensitivity, equivalent to 0.005 µIU/mL (Figure 6). The data are well represented by a four-parameter logistics fit to the dose-response, demonstrating a dynamic range over three decades; 1-1000 pg/mL

Figure 6. Analytical sensitivity using clinical samples is sub 1 pg/mL.



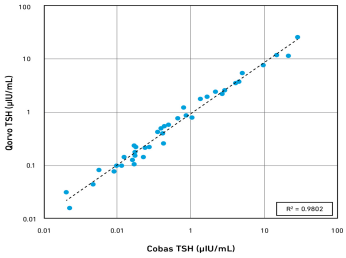
The level of Quantification (LOQ) of the hTSH assay is 1.5 pg/mL, equivalent to 0.018 µIU/mL, (Figure 7) within the central lab range of 0.010-0.020 µIU/mL (6).

Figure 7. LOQ for the hTSH assay on the Qorvo Biotechnologies System. Typical central lab levels shown in red box [6].



The platform was compared against the Roche Cobas e601 analyzer, resulting in r^2=0.98 correlation (Figure 8).

Figure 8. Predicate-matched data in human serum using the Roche Cobas e601.



Conclusion

The Qorvo Biotechnologies' hTSH assay on the investigation platform intersects central laboratory sensitivity with point-of-care ease of use and time to result based on the data collected to date. The platform has the promise of providing clinicians with ultra-high sensitivity, competitive LOQ, and a form factor that minimizes space and routine maintenance costs. The potential now exists to create a paradigm shift in point-of-care applications such as cardiac marker, bacterial/viral and infectious diseases.

References

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6. LoQ from package insert (metric varies by manufacture) adapted from: Clin Chem 63:7, 1248-1260 (20)