MODELING AND CONTROL OF QUARTZ CRYSTAL OPERATED IN LIQUID FOR BIO-SENSING APPLICATION

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ABSTRACT

Nowadays the applications of sensors are a very promising research field since they find application in many different areas. Biosensors are an increasingly important technology in the detection of compounds ranging from pesticides to biological weapons. Typically, biosensors consist of a biological macromolecule that is immobilized on the surface of a signal transducer. As the macromolecule binds specifically to the ligand being detected, the signal transducer can measure a physical change due to the binding event. One promising type of detector is the Quartz Crystal Microbalance (QCM). The QCM is a piezoelectric mass-sensing device. A QCM device works by sending an electrical signal through a gold-plated quartz crystal, which causes a vibration at some resonant frequency. The QCM then measures the frequency of oscillation in the crystal. When used as a biosensor, the QCM can detect changes in frequency of the crystal due to changes in mass on the surface of the crystal. In the present work, all related equations and data base related to biosensors piezoelectric devices will be considered in the developed model. The model will describe biosensors limitations and capacities together with measurement resolutions and errors. The work will includes build of software program using Microsoft visual studio C# 2010.net frame work 4.0 and all available theoretical and empirical formulas and program data base will include the data for QCM sensors and resonance frequencies, this program will include all cases needed to be studied for the present work (bio sensing). Many sensors can be used for QCM, the present work will be limited to TSM sensors, and the proposed software for Bio-sensing. The frequency signal is detected by a frequency counter and processed electronically in a separate computer. The QCM sensor used is 19.5 MHZ using buffer media in the testing procedure. The result according to z-methods indicates that while the resonance frequencies increase the small amount of despite material can be easily detected. With the data extracted for (5 MHZ) sensors with effective area of 14 mm^2, the results show that as the change in resonance frequency increase as the despite material increase. The film thickness of deposit material increase as the natural frequencies of sensors decreased.

ABSTRAK

Aplikasi sensor pada masa kini merupakan salah satu cabang penyelidikan yang boleh diaplikasikan dalam pelbagai bidang. Bio-sensor merupakan teknologi penting dalam mengesan campuran samada terdiri daripada racun perosak mahupun senjata biologi. Kebiasaannya, biosensor ini terdiri daripada makromolekul biologi yang mampu bergerak di permukaan transduser isyarat. Apabila makromolekul yang mengikat ligan dikesan, transduser isyarat akan mengesan perubahan dan mengukur perubahan fizikal yang disebabkan proses peyatuan tersebut. Transduser biasanya mengesan perubahan dalam rintangan, pH, haba, cahaya, atau jisim dan kemudiannya menukar data tersebut kepada isyarat elektrik untuk dikumpul dan diproses .Salah satu jenis pengesan adalah “Quartz Crystal Microbalance” (QCM). QCM ini ialah sejenis peranti pengesan piezoelektrik yang berfungsi menghantar isyarat elektrik melalui kristal kuarza yang disaluti emas dan kemudian menyebabkan getaran pada frekuensi salunan. Kemudian QCM akan mengukur kekerapan ayunan dalam kristal. QCM juga boleh berfungsi sebagai biosensor bagi mengesan perubahan frekuensi kristal yang disebabkan oleh perubahan jisim di permukaan kristal tersebut. Kajian ini juga merangkumi pembinaan perisian dengan menggunakan Microsoft visual studio C# 2010.net frame work 4.0 serta kesemua teori dan formula-formula empirikal serta program pangkalan data termasuk data-data untuk pengesan QCM dan salunan frekuenci. Program ini juga akan mengambil kira semua kajian berkenaan dengan bio-sensing. Walaupun terdapat banyak jenis pengesan yang boleh digunakan untuk QCM, namun kajian ini akan mengehadkan focus terhadap pengesan jenis TSM dan perisian yang dicadangkan untuk bio-sensing. Isyarat frekuensi yang dikesan pengira kekerapan akan diproses secara elektronik di computer yang berbeza. Pengesan QCM yang digunakan ialah 19.5 MHZ dan menggunakan media disambiguasi pada prosedur pengujian. Hasil kajian menurut kaedah-z menunjukkan peningkatan salunan frekuensi dalam jumpah yang kecil boleh dikesan dengan mudah. Data-data yang diekstrak (5MHZ) untuk pengesan pada luas efektif sebanyak 14 mm^2 menunjukkan perubahan salunan frekuensi meningkat ketika bahan deposit meningkat. Ketebalan filem bahan deposit juga meningkat apabila frekuensi asli pengesan berkurangan.

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LIST OF ABBREVIATION AND SYMBOLS

Δf	the observed frequency change, in Hz
Δm	the change in mass per unit area, in g/cm^2
Cf	the sensitivity factor for the crystal
n	number of the harmonic at which the crystal is driven
f_o	the resonant frequency of the fundamental mode of the crystal, in Hz
ρ_q	density of quartz – 2.648 g cm^{-3}
μ_q	shear modulus of quartz - 2.947.1011 $g.cm^{-1}.s^{-2}$
ρ_f	density of film material, in g/cm3
T_f	thickness of the film, in cm
f_u	frequency of oscillation of unloaded crystal
ρ_q	density of quartz – 2.648 g . cm^{-3}
μ_q	shear modulus of quartz- 2.947.1011 $g.cm^{-1}.s^{-2}$
ρ_L	density of the liquid in contact with the electrode
η_L	viscosity of the liquid in contact with the electrode
D	Dissipation factor
R_m	motional series resonance resistance, in Ω
Vc	conductance voltage output, in V
Nq	Frequency Constant for AT-cut quartz crystal: 1.668*1013 Hz. Å
ρq	density of quartz: 2.648 g . cm^{-3}
ρf	density of film material, in g . cm^{-3}
fU	Frequency of unloaded crystal (prior to deposition), in Hz
fL	Frequency of loaded crystal, in Hz
μq	shear modulus of quartz: 2.947.1011 g . cm^{-1} . s^{-2}

μf	shear modulus of film material
E_{lost}	the energy lost (dissipated) during one oscillation cycle
E_{stored}	the total energy stored in the oscillator.
fk	the series resonance frequency
$f\lambda$	the parallel resonance frequency
$Y(\omega)$	the total impedance in frequency domain
G	real part of admittance
B	imaginary part of admittance
Zm	Uncoated admittance (Rm, Cm, Lm, Cp)
Zv	Coated admittance (R1, L1)

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CHAPTER 1

INTRODUCTION

1.1 Project Background

The technical formula of Quartz-crystal is SiO_2 and it is composed of two elements, silicon and oxygen. In its amorphous form SiO_2 is the major constituent in many rocks and sand. The crystalline form of SiO_2 or quartz is relatively abundant in nature, but in the highly pure form required for the manufacture of quartz crystal units, the supply tends to be small.

The limited supply and the high cost of natural quartz have resulted in the development of a synthetic quartz manufacturing industry. Synthetic quartz crystals are produced in vertical autoclaves. The autoclave works on the principle of hydrothermal gradients with temperatures in excess of 400 °C and pressures exceeding 1,000 atmospheres [1]. Seed quartz crystals are placed in the upper chamber of the autoclave with natural quartz being placed in the lower chamber. An alkaline solution is then introduced which when heated increases the pressure within the chamber. The autoclave heaters produce a lower temperature at the top chamber in comparison to the bottom. This temperature gradient produces convection of the alkaline solution which dissolves the natural quartz at the bottom of the chamber and deposits it on the seed crystals at the top. Alpha crystals produced by this method can have masses of several hundred grams and can be grown in a few weeks. If the temperature reaches 573 °C a phase transition takes place which changes the quartz from an alpha to a beta (loss of piezoelectric property).

Quartz crystals are an indispensable component of modern electronic technology. They are used to generate frequencies to control and manage virtually all communication systems. They provide the isochronous element in most clocks, watches, computers and microprocessors. The quartz crystal is the product of the phenomenon of piezo-electricity discovered by the Curie brothers in France in 1880 [1].

1.2 Problem Statements

One of very promising applications of acoustic wave sensors is the measurement of small amounts of chemical and biological substances in liquids. A high sensitivity regarding mass loading is expected to be achieved due to the usage of shear waves because of their low interaction with the contacting fluid. As a consequence of their extraordinary properties quartz resonators can be found in all kinds of electronic devices, such as watches and computers to give an accurate time base, and as signal generators of reference systems in electronic devices.

Quartz resonators did not become of interest commercially until immediately prior to the world war. The development of new measurement technique represents one of the major driving forces in biotechnology that positively impact related research areas such as polymer characterization and biochemistry and is critical to the evolution of the pharmaceutical, biotechnology and biomaterial industries. Piezoelectric effect is a reversible of generation of internal electrical charges (or electrical field) in response to mechanical deformation of the material, or vice versa. Typically piezo sensors operate in dry conditions either in gases or a vacuum and are based on direct relationship of added mass and oscillation frequency given Sauerbrey equation.

Quartz crystal microbalance (QCM) sensors have become a valuable tool for the study of material properties with respect to fluids or solid films. The spectrum of applications related to the use of QCM sensors is continuously broadening, as it is evident from the ever increasing body of published articles in interdisciplinary scientific areas such as thin film materials, electrochemistry, and biosensors [2].

1.3 Project Objectives

This study embarks on the following objectives:

1. To study quartz crystal microbalance system, characteristics and properties.

2. To investigate the impedance spectra for AD Biomarker and Beta Amyloid 1-42 peptide antibodies using a developed modeling software.

3. To control the physical properties of the crystal based on the impedance characteristics by using Butterworth Van dyke (BVD) modeling software.

1.4 Project Scopes

The scopes of this project are comprise the boundaries of project study. Many scopes should be bound in order to make this project achieve the objectives.

1. Develop a mathematical model for quartz crystal system, Crystal oscillation ranged between 5 to 30 MHZ.

2. Simulate the quartz crystal microbalance system by develop a suitable modeling software.

3. Control physical properties of crystal by Butterworth Van dyke (BVD) equivalent circuit using suitable software and get impedance characteristics for different quartz crystal frequencies overtones.

1.5 Research Significance

The advantages that the QCM provides for development of the above domain areas is a sensitive detection capability for surface mass binding and a surface viscoelastic characterization capability for the bound mass, other distinct advantages of the QCM technique are the following:

1. The mass sensing technique eliminates the need for any specific labeling step to be part of the signal transduction mechanism.

2. Signal transduction via the piezoelectric mechanism operates well in complex, often optically opaque solution media.

3. The technique is capable of detecting subtle changes in the solution-surface interface that can be due to density-viscosity changes in the solution, viscoelastic changes in the bound interfacial material, and changes in the surface free energy, to name a few.

4. The electrochemical quartz crystal microbalance (EQCM) variant allows the investigator to apply a potential on the upper metal electrode, thereby creating an electrochemical cell, enabling electro chemical reactions or measurement of processes involving electron transfer. This provides interesting ways to create or probe surface bound mass as we describe in this review.

5. Finally, the technique is relatively easy to use, and the basic equipment is inexpensive to purchase. Although the QCM will not supplant high throughput array technologies for drug or biomaterials screening, it provides the realistic possibility of low throughput arrays, perhaps useful in secondary screening situations.

In this format, the QCM provides interesting ways to characterize the mass and visco-elastic properties of complex thin biopolymer films incorporating bimolecular systems at surfaces in the solution of choice, both during their formation and once formed and under perturbations in their environment.

Thus, the QCM technique becomes a useful adjunct to the development of future non-QCM array technologies. It has found use already as a gas phase chemical sensor and metal deposition sensor in vacuum applications and is being developed as a biosensor platform.

For these reasons, the technique is currently exhibiting rapid growth outside of its traditional development domain area of analytical chemistry and electro analytical chemistry.

A number of review articles have appeared in recent years that discuss the applications and technical issues involved in QCM use. They range from the perspective of QCM as a fundamental tool in analytical electrochemistry to comparative reviews focused on the newer application areas of biosensors and drug discovery.

In this review the concentrate is on the application of the QCM technique to the study of the formation and characterization of thin but complex biopolymer meric films and biomimetic systems involving biomacromolecules and briefly outline its applications to the study of fundamental biological processes, biosensors for analyte detection, and more complex biomolecular systems, including living cells [3], this study having the following applications listed in Table 1.1.

Table 1.1: QCM Applications [9]

<table>
<tr>
<td>Military & Aerospace
Communications
Navigation
IFF
Radar
Sensors
Guidance systems
Fuzzes
Electronic warfare
Sonobouys</td>
<td>Research & Metrology
Atomic clocks
Instruments
Astronomy & geodesy
Space tracking
Celestial navigation</td>
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Communications
Telecommunications
Mobile/cellular/portable radio, telephone & pager
Aviation
Marine
Navigation
Instrumentation
Computers
Digital systems
CRT displays
Disk drives
Modems
Tagging/identification
Utilities
Sensors</td>
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<td>Automotive
Engine control, stereo, clock
Trip computer, GPS</td>
<td>Consumer
Watches & clocks
Cellular & cordless phones, pagers
Radio & hi-fi equipment
Color TV
Cable TV systems
Home computers
VCR & video camera
CB & amateur radio
Toys & games
Pacemakers
Other medical device</td>
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1.6 Summary

Quartz crystals (SiO_2) are an indispensable component of modern electronic technology. They are used to generate frequencies to control and manage virtually all communication systems. It is the product of the phenomenon of piezo-electricity discovered by the Curie brothers in France in 1880.

Quartz crystal microbalance (QCM) sensors have become a valuable tool for the study of material properties with respect to fluids or solid films. The spectrum of applications related to the use of QCM sensors is continuously broadening, as it is evident from the ever increasing body of published articles in interdisciplinary scientific areas such as thin film materials, electrochemistry, and biosensors. Many scopes should be bound in order to make this project achieve the objectives including Derive the equations of liquid cell for single sided AT cut quartz crystal.

Crystal oscillation ranged between 5 to 30 MHZ , Simulate the liquid cell for single sided AT cut quartz crystal with Butterworth Van dyke (BVD) modeling software, a lower sensitivity limit for QCM device will be examined , and Calibrate physical properties of crystal by using suitable software to get impedance characteristics for different quartz crystal thickness and frequencies overtones. In this project we expect that Mass sensitivity increases with increasing frequency (f) of crystal oscillation , Higher frequency (f) crystals that are significantly more mass sensitive increases the effect surface area of the device, utilizing the piezoelectric mechanism in novel ways, and creating higher throughput multiwall devices for commercial applications , and an increase in motional resistance decreases the frequency(f).

CHAPTER 2

LITERATURE REVIEW

2.1 Introduction

In the last decade, a new analytical method for the in situ investigation of interfacial processes, including electrode processes, has emerged. This method, commonly referred to as the quartz crystal microbalance (QCM), has had a significant impact in numerous research programs. This includes electrochemists, for which the method is referred to as the electrochemical quartz crystal microbalance (EQCM).

These methods rely on the piezoelectric properties of quartz, in particular a single crystal of quartz that has been cut into a thin wafer at an angle of approximately 35 degrees with respect to the polar z-axis of quartz. The word piezoelectric derives from the word piezein, meaning to press. Hence, the piezoelectric effect hinges on "pressure electricity," a phenomenon first observed by Jacques and Pierre Curie when they discovered that mechanical stress applied to the surfaces of certain crystals, including quartz, resulted in an electrical potential across the crystal.

Shortly afterward, the converse piezoelectric effect – a mechanical strain produced by application of an electric potential across the crystal – was discovered. This effect is sometimes referred to as the converse piezoelectric effect. The motor generator properties have long been associated with underwater sound transducers (sonar), and electromechanical devices such as speakers, microphones, and phonograph pickups.

The quartz crystal microbalance earns its name from its ability to measure the mass of thin films that have adhered to its surface. The quartz crystal microbalance generally comprises a thin AT-cut quartz wafer with a diameter of (0.25 - 1.0) inches, sandwiched between two metal electrodes which are used to establish an electric field across the crystal. If an alternating electric field and appropriate electronics are used, the crystal can be made to oscillate at its resonant frequency. Most crystals of current interest resonate between (5 to 30 MHz).

The measured frequency is dependent upon the combined thickness of the quartz wafer, metal electrodes, and material deposited on the quartz crystal microbalance surface. Because the resonance is very sharp, high precision frequency measurements allow the detection of minute amounts of deposited material, as small as 100 picograms on a square centimeter. Mass changes occurring at the QCM surface result in frequency changes according to the well-established Sauerbrey equation, named after the pioneer of this technique for measurement of film thickness.

The signal transduction mechanism of the QCM technique relies upon the piezoelectric effect in quartz crystals, first discovered in 1880 by the Curie brothers, via a pressure effect on quartz. A change in inertia of a vibrating crystal was then shown by Lord Rayleigh to alter its resonant frequency, f. important subsequent developments were good crystal stability through the use of electric resonators and room-temperature stable AT-cut crystals. In 1959, the QCM was first used in a sensing mode when Sauerbray reported a linear relationship between the f decrease of an oscillating quartz crystal and the bound elastic mass of deposited metal.

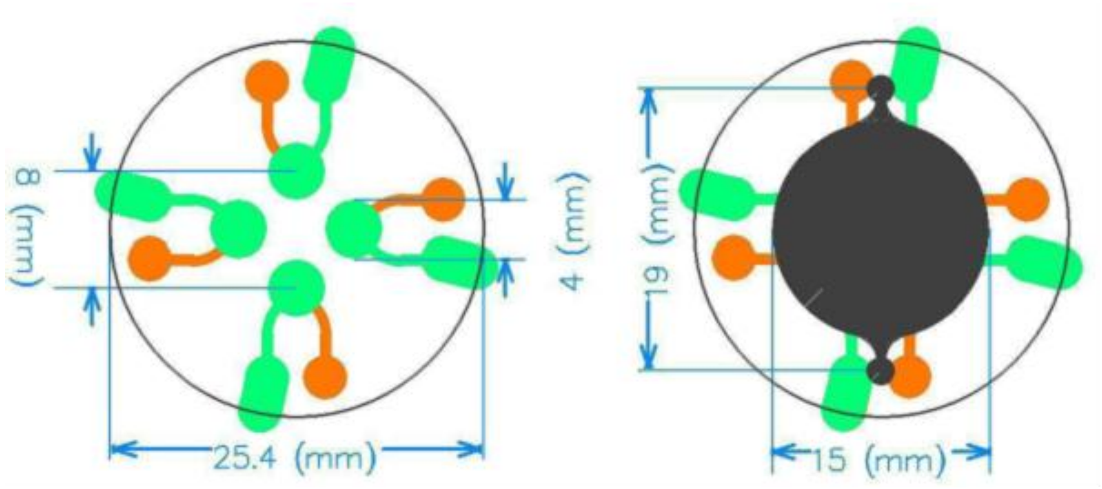
Early chemical applications of QCM were to measuring mass binding from gas-phase species to the quartz surface. These represented some of the earliest chemical sensors for moisture and volatile organic compounds, and gas-phase chromatography detectors. In the 1980s, solution based QCM developed as new oscillator technology advanced to measure changes in frequency that could be related to changes in viscosity and density in highly damping liquid media.

The recent success of the QCM technique is due to its ability to sensitively measure mass changes associated with liquid-solid interfacial phenomena, as well as to characterize energy dissipative or viscoelastic behavior of the mass deposited upon the metal electrode surface of the quartz crystal. Anything that has mass can generate a response from a QCM sensor.

The universal response of the device is the reason for the wide range of application of the technology. However, the downside of such universal sensitivity is that you always have a great danger of interferences. For analytical purposes, it is imperative to find ways of getting the QCM sensor to respond only to what you are interested in (i.e. build sensitivity into the device). This usually involves the addition of a sensitive layer on the surface of the crystal [4]. Organic polymers comprise the most common type of coating used with QCM sensors due to their capability to reversibly sorb vapors and liquids [5].

The relative importance of the mass-loading and viscoelastic contributions of the film to the observed QCM response is a subject that has yet to be resolved. In no area have the QCM applications seen such dramatic increase in recent years as in the field of biochemical analysis. QCM devices are routinely used as biochemical and immunological probes [6], as well as for the investigation and/or monitoring of biochemically significant processes. Sensitive, selective detection of biochemically active compounds can be achieved by employing antigen antibody [7], enzyme substrates and other receptor –protein pairs. The potential analytical use of these materials has been reviewed, particularly with respect to the development of biochemical sensors [8].

QCM studies have provided detailed information about the functionalized surfaces developed for a range of biochip and biosensor applications.As example of QCM sensors was fabricated on a single disc of 1-inch (5 MHz) AT-cut quartz crystal sub-strate. The number of QCM sensors on a quartz sub-strate was designed as 4 and the patterns of electrode pair were laid out symmetrically within 1-inch circle as illustrated in Figure 2.1 [9], and the biological sensing method shows in Figure 2.2.



(a) (b)

Figure 2.1: Schematic of QCM sensor array (a) electrode layout and (b) electrodes superimposed by PDMS

2.2 QCM Systems

QCM Systems are applied routinely by biologists and biochemists to obtain information about processes such as:

1. protein adsorption/desorption [10],
2. cell adhesion [11],
3. Protein-protein interaction,
4. Degradation of polymers,
5. bio fouling and bio film formation,
6. drug analysis [12] and
7. DNA Biosensors.

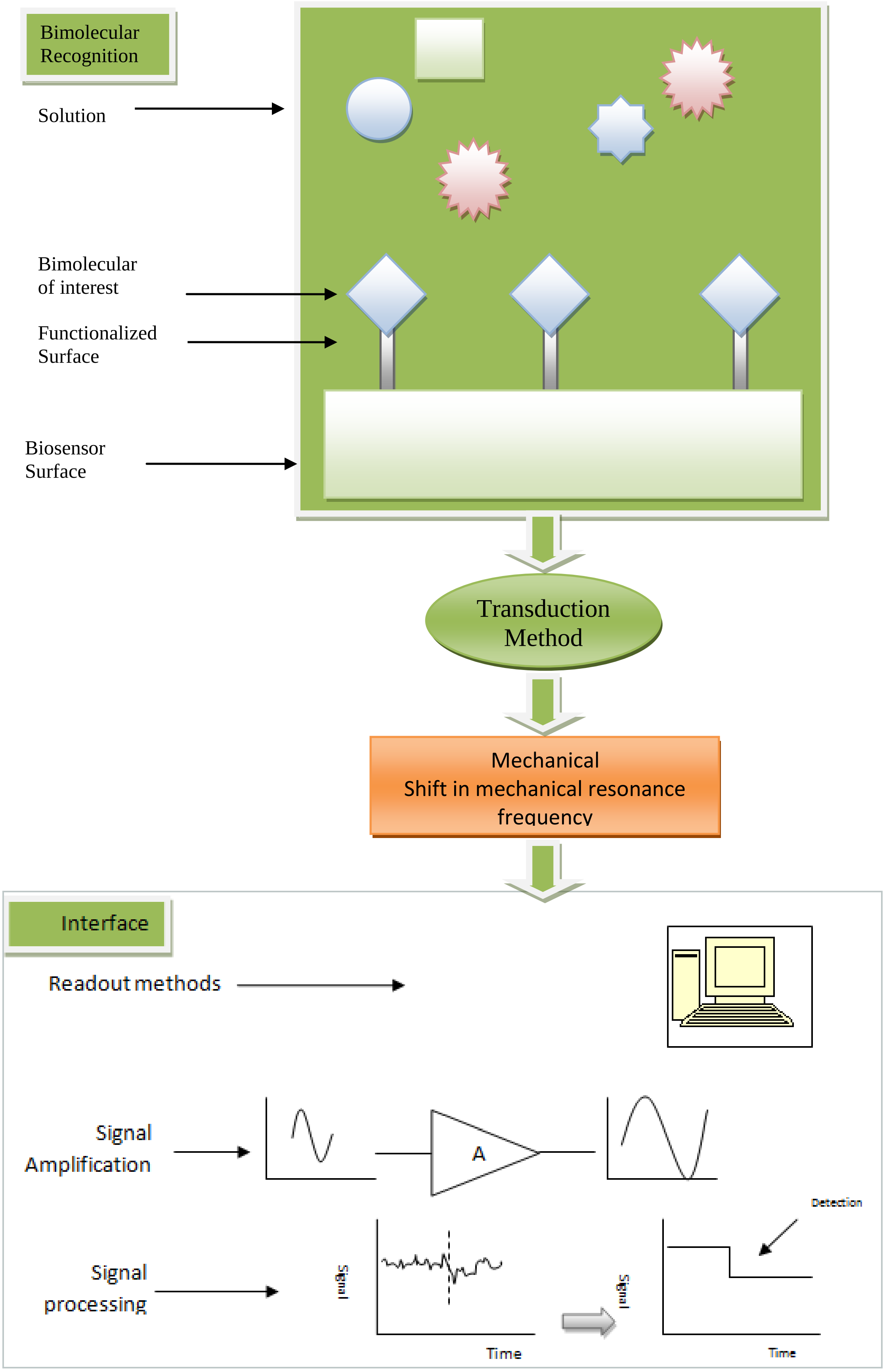


Figure 2.2: Biological sensing method

2.3 Quartz Characteristics

Quartz is the only material known that possesses the following Combination of properties:

1. Piezoelectric ("pressure-electric"; piezein = to press, in Greek)
2. Zero temperature coefficient cuts exist
3. Stress compensated cut exists
4. Low loss (i.e., high Q)
5. Easy to process; low solubility in everything, under "normal" conditions, except the fluoride etchants; hard but not brittle
6. Abundant in nature; easy to grow in large quantities, at low cost, and with relatively high purity and perfection. Of the man-grown single crystals, quartz, at ~3,000 tons per year, is second only to silicon in quantity grown (3 to 4 times as much Si is grown annually, as of 1997).

2.4 Previous Studies

Steven J. Lasky and Daniel A. Buttry (1989), fabricated a biosensor based on the use of the QCM for glucose detection using hexokinase immobilized within a poly (acrylamide) matrix. Very large frequency changes accompany the binding of glucose to the enzyme. The frequency changes are quite reproducible for a given crystal. The signal to noise level is in excess of 100 for a glucose concentration of 10 mM, a value close to that found in blood (ca. 7 mM). These frequency changes appear to be too large to arise solely from the mass change due the binding reaction. Two possible mechanisms for the production of such unexpectedly large frequency changes have been discussed, and experiments proposed to determine their applicability to the observations.

Gabriel Ohlsson and Christoph Langhammer, (1991), discovered a novel device for nanometer-confinement of soft matter in one dimension (1D). This nanocell, with very large (up to 10(6):1) cell-radius to cell-height ratio, is tailored as an accessory for quartz crystal microbalance (QCM) and QCM with dissipation-monitoring (QCM-D) sensing , they studied internal and interfacial energy dissipation phenomena in highly confined (in 1D) soft matter and fluid films (patent pending).

The cell consists of two macroscopic plates (diameter of 9 mm), a top (the "lid") and a bottom (the QCM-D sensor), separated by appropriate spacers with heights ranging from below 100 nm up to 10 microm. The surfaces of both the lid and the bottom plate can be mechanically or/and chemically modified, prior to cell assembly, in order to tailor desired interfacial properties for the experiment. The cell is mounted on a standard QCM-D sensor, an AT-cut quartz crystal (the quartz crystal is cut at an angle of 35 degrees from its ZX-plane), forming the bottom plate. We illustrate theoretically and experimentally, as application examples, the use of this device for studies of dynamic mass loading and internal energy dissipation processes in thin films of ethylene glycol respective thin liquid crystal films around the nematic-isotropic phase transition.

Tatsuro Goda et.al, (2012), developed an integrated device comprising a quartz crystal microbalance (QCM) and a field-effect transistor (FET) with a single common gold electrode in a flow chamber. An alternating current inducing oscillations in the piezoelectric quartz of the QCM sensor is electrically independent of the circuit for the FET output so that the two sensors in different detection mechanisms simultaneously record binding kinetics from a single protein solution on the same electrode.

A conjunction of adsorbed mass from QCM with electric nature of bound protein from FET provided deeper understanding on a complex process of nonspecific protein adsorption and subsequent conformational changes at a solid/liquid interface.

Lower apparent k (on) values obtained by FET than those obtained by QCM on hydrophobic surfaces are interpreted as preferred binding of protein molecules facing uncharged domains to the electrode surface, whereas higher k (off) values by FET than those by QCM imply active macromolecular rearrangements on the surfaces mainly driven by hydrophobic association in an aqueous medium. The advanced features of the combined sensor including in situ, label-free, and real-time monitoring provide information on structural dynamics, beyond measurements of affinities and kinetics in biological binding reactions.

Z Parlak,et.al, (2013), described the physical understanding of a method which differentiates between the frequency shift caused by fluid viscosity and density from that caused by mass adsorption in the resonance of a quartz crystal resonator.

This method uses the normalized conductance of the crystal to determine a critical frequency at which the fluid mass and fluid loss compensates each other. Tracking the shift in this critical frequency allows us to determine purely mass adsorption on the crystal. They extended this method to Maxwellian fluids for understanding the mass adsorption in non-Newtonian fluids. They validate our approach by real-time mass adsorption measurements using glycerol and albumin solutions.

2.5 Summary

The success of the QCM technique is due to its ability to sensitively measure mass changes associated with liquid-solid interfacial phenomena, as well as to characterize energy dissipative or viscoelastic behavior of the mass deposited upon the metal electrode surface of the quartz crystal.

QCM studies have provided detailed information about the functionalized surfaces developed for a range of biochip and biosensor applications. As example of QCM sensors was fabricated on a single disc of 1-inch (5 MHz) AT-cut quartz crystal sub-strate. Steven et al. fabricated a biosensor based on the use of the QCM for glucose detection using hexokinase immobilized within a poly (acrylamide) matrix.

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CHAPTER 3

METHODOLOGY

3.1 Introduction

The piezoelectric transducers allowed a binding event to be converted into a measurable signal, (resonance frequency changes). The principle was based on the piezoelectric properties of quartz crystals. Piezoelectric devices were developed based on this principle. When it was included in an appropriate electronic circuit, the measured oscillation frequency was closed to the resonant frequency and the generated wave amplitude reached a maximum. Thus, a modification of a physical characteristic of the resonator, (the global mass or the thickness), led to a resonant frequency variation. For biosensors, mass changes, occurring from the interaction between the modified transducer surface and a detected species can be measured by this way. Several piezoelectric devices were developed based on this principle.

In the present work, all related equations and data base related to biosensors piezoelectric devices will be considered in the developed model. The model will describe biosensors limitations and capacities together with measurement resolutions and errors; the project flow chart is shown in Figure 3.1.

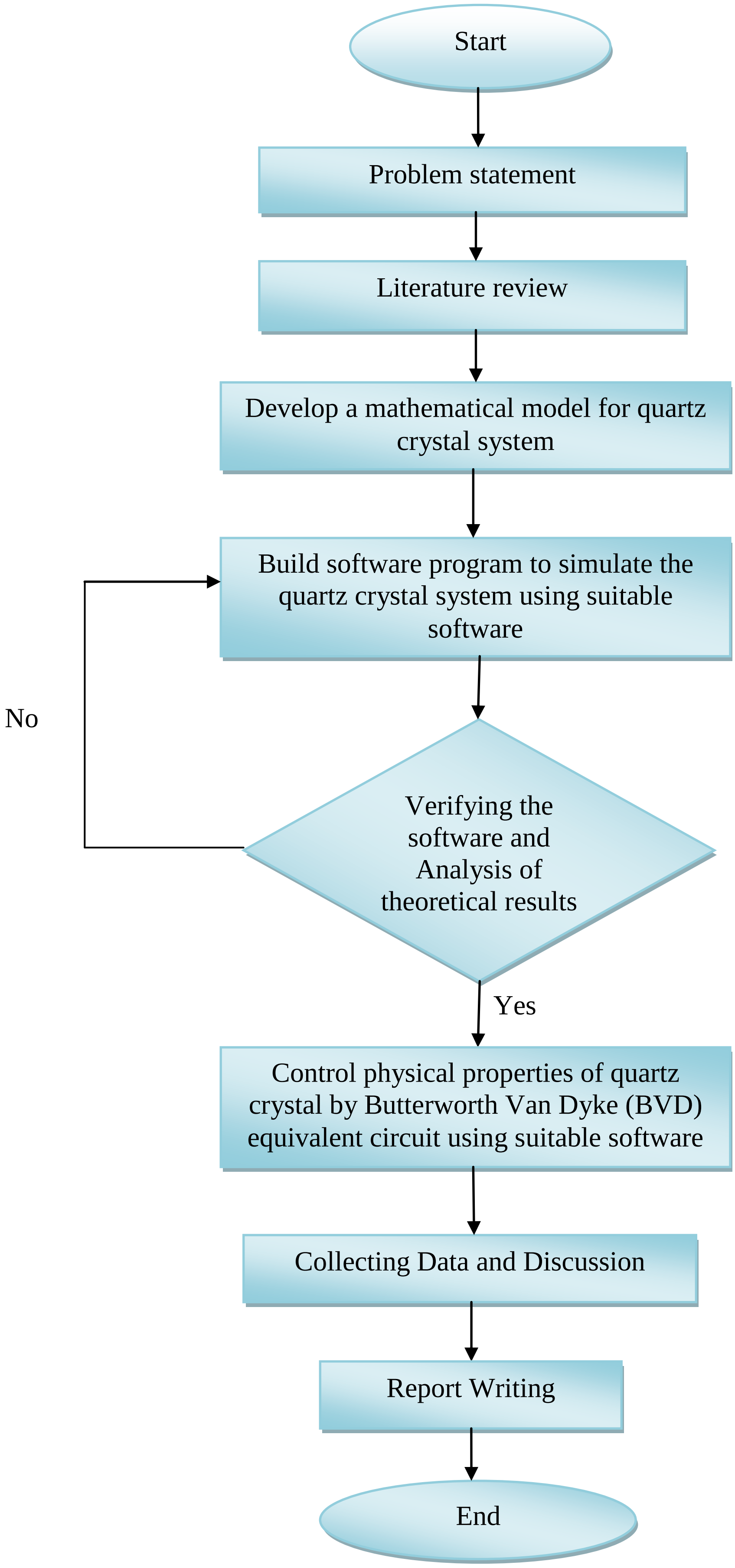

Figure 3.1: Flow chart of the project

Sauerbrey [17] was the first to recognize the potential usefulness of the Quartz Crystal Microbalance (QCM) technology and demonstrate the extremely sensitive nature of these piezoelectric devices towards mass changes at the surface of QCM electrodes. The results of his work are embodied in the Sauerbrey equation, which relates the mass change per unit area at the QCM electrode surface to the observed change in oscillation frequency of the crystal:

$$\Delta f = - Cf \,.\, \Delta m \qquad (3.1)$$

Where,

Δf - the observed frequency change, in Hz,

Δm - the change in mass per unit area, in g/cm2, and

Cf- the sensitivity factor for the crystal used (i.e. 56.6 Hz μg^{-1}cm2 for a 5MHz AT-cut quartz crystal at room temperature.)

The Sauerbrey equation relies on a linear sensitivity factor, Cf, which is a fundamental property of the QCM crystal. Thus, in theory, the QCM mass sensor does not require calibration. However, it must be kept in mind, that the Sauerbrey equation is only strictly applicable to uniform, rigid, thin-film deposits [18].

Vacuum and gas phase thin-film depositions which fail to fulfill any of these conditions actually exhibit more complicated frequency-mass correlations and often require some calibration to yield accurate results.

Sauerbrey's equation (Equation 3.1) is often used to calculate mass loadings and thin-film thicknesses in vacuum depositions. The basic assumption is that the incremental change in mass from the foreign film is treated as though it were really an extension of the thickness of the underlying quartz, the foreign film is considered rigid and so thin that it does not experience any shear forces during vibration.

As a result, the sensitivity factor, Cf, is a fundamental property of the quartz crystal and does not consider any of the properties of the foreign film (i.e. it is only dependent on the acousto-elastic properties of quartz.)

$Cf = 2nf_o^2/(\rho_q\mu_q)^{1/2}$ (3.2)

Where,

n - number of the harmonic at which the crystal is driven,

f_o - the resonant frequency of the fundamental mode of the crystal, in Hz,

ρ_q - density of quartz – 2.648 g cm^{-3}, and

μ_q - shear modulus of quartz - 2.947.1011 $g.cm^{-1}.s^{-2}$

The dependence of the frequency change on the mass coverage per unit area emphasizes the fact that, within certain limits, the sensitivity factor is independent of the electrode geometry. Thus, in theory, the QCM mass sensor does not require calibration for this application. This ability to calculate mass loading from first principles is obviously a very active feature of these devices. Film thickness is often the parameter of interest in gas-phase thin-film depositions. If the mass coverage is believed to be uniform, the thickness of the film is easily calculated dividing the mass per unit area provided by Sauerbrey's equation by the material's density:

$T_f = \Delta m / \rho_f$ (3.3)

Where,

ρ_f - density of film material, in g/cm3,

Δm - change in mass per unit area, in g/cm2 (calculated from Sauerbrey's equation),

T_f - Thickness of the film, in cm.

Until recently, it was believed that excessive viscous loading would prohibit use of the QCM in liquids. In fact, operation in liquids is indeed possible [19], and the response of the QCM is still extremely sensitive to mass changes at the solid solution interface.

For many years, QCMs have been used in direct contact with liquids and/or viscoelastic films to assess changes in mass and viscoelastic properties during chemical and electrochemical surface processes. When the QCM comes in contact with a solution, there is a decrease in frequency that is dependent upon the viscosity and the density of the solution. A quantitative understanding of the resonator behavior is a prerequisite for proper interpretation of experimental results under total liquid immersion. This problem was first treated by Glassford [20], and later by Kanazawa and Gordon [21].

Kanazawa's treatment of the influence of the solution properties on the crystal (equation 3.4) permits the prediction of the change in resonance frequency which accompanies immersion of the crystal into a viscous medium:

$$\Delta f = - f_u^{3/2} . [(\rho_L \eta_L)/ (\pi . \rho_q \mu_q)]^{1/2} \tag{3.4}$$

Where,

f_u - frequency of oscillation of unloaded crystal,

ρ_q - density of quartz – 2.648 g . cm^{-3},

μ_q - shear modulus of quartz- 2.947.1011 $g.cm^{-1}.s^{-2}$,

ρ_L - density of the liquid in contact with the electrode, and

η_L - viscosity of the liquid in contact with the electrode.

Viscous coupling of the liquid medium to the oscillating crystal surface results not only in a decrease in the series resonant frequency but also in damping of the resonant oscillation- the viscous loss is manifested as an increase in series resonance resistance, R, of the QCM resonator. Thus, R serves as an excellent independent measure of viscous loading by the medium (liquid or soft-film) at the crystal's surface.

3.2 Dissipation factor (D)

A film that is "soft" (viscoelastic) will not fully couple to the oscillation of the crystal; hence the Sauerbrey relation will underestimate the mass at the surface. A soft film dampens the sensor's oscillation. The damping or energy dissipation (D) of the sensor's oscillation reveals the film's softness (viscoelasticity) so that energy dissipated per oscillation/2π total energy stored in system, D is defined as:

$$D = E_{lost} / 2\pi E_{stored} \quad (3.5)$$

Where,

D - energy dissipation

E_{lost} - the energy lost (dissipated) during one oscillation cycle and

E_{stored} - the total energy stored in the oscillator.

3.3 Resistance Measurement

The QCM100 Analog Controller provides a Conductance 7 Voltage output (BNC port), that is related to the crystal's motional series resonance resistance:

$$R_m = 10{,}000 \cdot 10^{-Vc/5} - 75 \quad (3.6)$$

Where,

R_m - motional series resonance resistance, in Ω

Vc - conductance voltage output, in V.

3.4 Errors in the measurement of R_m

Errors in the measurement of R_m will be less than 3Ω + 3% of R_m (for $R_m < 2k\Omega$), and are dominated by the departure of the voltage controlled attenuator from its nominal (voltage, gain) characteristic.

Keep also in mind that the resistance measurement in liquids and soft films is also affected by temperature, mostly through the temperature coefficient of the viscosity. For example, a 4Ω/°C drift in resistance is to be expected in water around room temperature.

3.5 Noise in the measurement of R_m

Vc varies logarithmically with R_m over most of the range of interest. There is an important advantage in this: the fractional resolution of the resistance is nearly independent of the resistance and so allows detailed and low- noise measurement of the viscous losses. To estimate the noise in resistance measurements, we can take the derivative of the equation for the motional resistance (units are Ohms and Ohms/Volt):

$$R_m = (10{,}000 \cdot 10\text{-}^{Vc/5} - 75)$$

$$d\,R_m / dVc = 10{,}000 \cdot 10^{-Vc/5} \cdot \ln(10) \cdot (-1/5) \qquad (3.7)$$

$$= -2{,}000 \cdot \ln(10) \cdot 10^{-Vc/5}$$
$$\approx -4605 \cdot 10^{-Vc/5}$$
$$\approx -0.4605 \cdot (R_m + 75)$$

Noise on the Vc signal, Δ Vc, is typically ± 50μV (with one second averaging). The R_m for a 5MHz crystal in water is about 375Ω. The fractional noise in the resistance measurement is then:

$$\Delta R_m / R_m = \Delta Vc \cdot [d R_m / dVc] / R_m \qquad (3.8)$$

$$= \Delta Vc \cdot [-0.4605 \cdot (R_m + 75)] / R_m$$
$$= \pm 28 \text{ ppm.}$$

This low noise floor for fractional resistance measurements allows very small changes in dissipation losses to be measured. This is also the reason why a high precision voltmeter (with at least six digits of resolution) is recommended for these measurements.

3.6 Calibration of R_m

Resistance measurements for the QCM25 Crystal Controller/QCM100 are calibrated by replacing the crystal with a precision resistor in parallel with a 15pF capacitor. Two resistor values are used: 51.10Ω and 1.000kΩ. The equation for R_m may be inverted to determine the calibration value for Vc. (Motional resistance, R_m, in Ω and conductance voltage output, Vc, in volts.)

$$R_m = (10{,}000 \cdot 10\text{-}Vc/5 - 75) \qquad (3.9)$$

$$Vc = 5 \log [10{,}000 / (R_m + 75)] \qquad (3.10)$$

The low pass filter is adjusted so that the QCM25 Crystal Controller oscillates at 5MHz with the 51.10Ω resistor in place of the crystal. The varactor dial is adjusted so that the Crystal Controller oscillates at 5MHz with the 1.000kΩ resistor in place of the crystal. Calibration potentiometers in the QCM25 Crystal Controller are adjusted so that Vc = 9.496Vdc with a calibration resistor of 51.10Ω, and so that Vc = 4.843Vdc with a calibration resistor of 1.000kΩ [22].

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