DEVELOPMENT OF MULTIPLEXED MICROCONTROLLER BASED SYSTEM FOR MICROBIOREACTOR

AHMAD YASER AL-HADDAD

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I dedicate this to the revolts of Syria, to my parents, who have been supportive throughout my life, to my grandparents, to my sisters, to my brothers, to all my teachers who have inspired me a lot.

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ABSTRACT

Bioreactor is a device that widely used in fermentation process. Bench scale bioreactor and shake flask are the most used devices to optimize such process. Due to their high running cost and the high amount of labour required, new and better alternative way must be found to carry on the optimization process. In the most recent years, scientists have been working on smaller bioreactor of volume less than 1 millilitre and became known as microbioreactor. This device and due to its small volume size should bring more benefits and potential to optimization process in fermentation. Since microbioreactor stills in development phase, researches till date are trying to come with ideas and designs to be adopted later as acceptable industry standard. In the literature, there have been many designs attempts to create a platform to support one or more microbioreactors. Many of these attempts have achieved great results with comparable performance to that of bench scale bioreactor. Most the previous designs are made with the usage of data acquisition card from National instrument. The trend toward NI DAQ is due to the simplicity in programming environment, being user friendly and many other features. Biochemical engineers could settle for alternative and cheaper way, if they are willing to give up some of the convenient and features provided by NI DAQ. In this project, this alternative method is being investigated, tested and used. The goal is to use microcontroller as DAQ to provide controlling, data logging and monitoring of temperature and speed control for microbioreactor. This setup will be totally microcontroller based and using dedicated electronic circuit to achieve the objectives. The results for temperature and agitation control that have been obtained are satisfactory and now this setup is ready to be used on actual microbioreactor.

ABSTRAK

Bioreaktor adalah alat yang digunakan secara meluas dalam proses penapaian. Bioreaktor skala jenis duduk dan kelalang digunakan secara meluas bagi tujuan pengoptimuman. Disebabkan kos pengoperasian dan jumlah tenaga kerja yang ramai diperlukan, kaedah alternative yang baru dan lebih baik diperlukan. Sejak beberapa tahun kebelakangan ini, saintis telah meneruskan kajian mereka menggunakan isipadu kurang dari 1 milimeter dan dikenali sebagai microbioreaktor. Peranti ini dan disebabkan oleh julat kerja yang kecil, ia sepatutnya memberikan kelebihan dan keupayaan tinggi untuk proses pengoptimuman dalam proses penapaian. Memandangkan proses mikrobioreaktor masih dalam fasa pembangunan, para penyelidik masih mengkaji idea-idea dan rekabentuk-rekabentuk yang baru untuk diadoptasi kemudiannya agar selari dengan standard industri. Dalam kajian yang dilakukan, terdapat banyak kajian rekabentuk dilakukan bagi tujuan untuk membina satu platform untuk menyokong satu atau lebih mikrobioreaktor. Kebanyakkan hasil kajian ini telah mencapai keputusan yang memberangsangkan jika dibandingkan dengan bioreactor skala jenis duduk. Kebanyakkan rekabentuk-rekabentuk asal dibina dengan menggunakan kad perolehan data (DAQ) dari National Semiconductor (NI). Trend masa kini ke arah penggunaan kad DAQ adalah disebabkan oleh mudahnya pengaturcaraan, mudah diguna, dan ciri-ciri yang lain-lain. Jurutera biokimia memiliki alternatif dan kaedah yang murah, sekiranya mereka sanggup mengorbankan kemudahan dan ciri-ciri yang disediakan oleh NI DAQ. Dalam projek ini, kaedah alternatif ini dikaji, diuji, dan digunakan. Matlamatnya adalah untuk menggunakan mikropengawal sebagai DAQ untuk membekalkan kawalan, perekodan data, dan pemantauan suhu dan kawalan kelajuan untuk mikrobioreaktor. Persediaan ini adalah berdasarkan mikropengawal sepenuhnya dan menggunakan litar elektronik untuk mencapai objektifnya. Keputusan bagi kawalan suhu dan pergolakan yang diperolehi adalah memuaskan dan persediakan ini adalah siap dan boleh digunapakai.

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LIST OF ABBREVIATIONS

DAQ	-	Data Acquisition Card
DO	-	Dissolved Oxygen
OD	-	Optical Density
NI	-	National Instruments
PID	-	proportional-integral-derivative
GUI	-	Graphical User Interface
rpm	-	revolution per minute
PMMA	-	polymethylmethacrylate
PDMS	-	polydimethylsiloxane
RTD	-	resistance temperature detectors
S/V	-	surface area to working volume ratio
ISFET	-	ion-sensitive and field-effect transistor
PWM	-	Pulse-width modulation
ADC	-	Analog Digital converter
PCB	-	printed circuit board
IC	-	integrated circuit

LIST OF SYMBOLS

mL	-	millilitre
µL	-	microlitre
°C	-	celsius
V	-	voltage/volts
mV	-	millivolt
µV	-	microvolt
A	-	ampere
mA	-	milliampere
Ω	-	ohms
µF	-	microfarad
Hz	-	hertz

CHAPTER 1

INTRODUCTION

1.1 Introduction to Bioreactors

A bioreactor as shown in Figure 1.1 is simply a vessel usually cylindrical in shape that used to carry out fermentation experiments. A bioreactor normally integrated with tight on line measurements and process control capabilities. These features are critically important such that fermentation experiments in bioreactor can be performed under controlled conditions as stated by Bailey *el. al (*1986). For a standard bioreactor system, it is norm to have a feedback control loop over physical parameters such as pH, temperature, agitation, dissolved oxygen concentration and water level.

Fermentation is a process that is widely performed in many sectors such as biotechnology, food processing, health care, agriculture and environmental management as stated by Szita N *el. al* (2005). They are many devices that are in use to optimize such processes for example bench scale bioreactors or shake flasks. These devices range in terms of the volume size and capabilities. Bench scale biroeactors normally operated between working volume of 1 liter and 10 liters where else shake flasks utilized much lower volume i.e. less than 2 liters. In relative to bench scale bioreactors, shake flasks usually do not integrated with sensors and actuators. Mixing is based on shaking principle and operation is generally limited to batch mode operation only.

In the most recent years, scientists have been attempting to create smaller bioreactor design that comprises the advantages of both types of experimental tools (shake flasks and bioreactor) in one small unit named as microbioreactor shown in Figure 1.2. The drastic reduction in volume's size to less than 1mL will reduce the cost dramatically and open the possibilities of running multi microbioreactors simultaneously (multiplexing) hence increasing the throughput. As stated by D. Schäpper *el. al* (2009) microbioreactor would not only reduce the fabrication cost per bioreactor compared to bench scale, but will also add more advantages such as reduced running cost through the reduction of substrate required, reduced power requirements, reduced space requirements especially in parallel operations and finally reducing the effort and labour required to prepare the bioreactor through the usage of disposable microbioreactors.

Even though dramatic cost reduction can be obtained using microbioreactors as previously mentioned, another part of the microbioreactor platform circuit design still suffering from high cost and still need to be considered. The circuit design includes all the necessary electrical components that are needed to interface and control the microbioreactor such as Data Acquisition Card (DAQ), temperature sensor transmitter and any possible actuators. Most of the work previously performed on microbioreactor such that by Szita N *el. al* (2005), M.N.H.Z Alam *el. al* (2010), D. Schäpper *el. al* (2010) and Lee HL *el. al* (2006) are all made using high end DAQ from National instrument. The trend toward NI DAQ is due to many features provided and the convenient when it comes to programming, but that comes with a price. Since many of the great capabilities and features of NI DAQ are being paid for and not being used, alternative and cheaper way could be used as replacement if giving up some of the convenience provided by NI DAQ is not an issue.

The aim of this project is to present cheaper and effective way with comparable results to replace the expensive and bulky circuitry that is usually used on microbioreactor design. Many of the devices around us are being incorporated with low-cost microcontroller into their circuitry design to perform many tasks effectively. Part of this project is to introduce the microcontroller into micobioreactor circuit design to replace the DAQ without dramatic lose in the performance. The microcontroller based DAQ should handle data logging, controlling and monitoring.

Figure 1.1 New Brunswick bioreactor

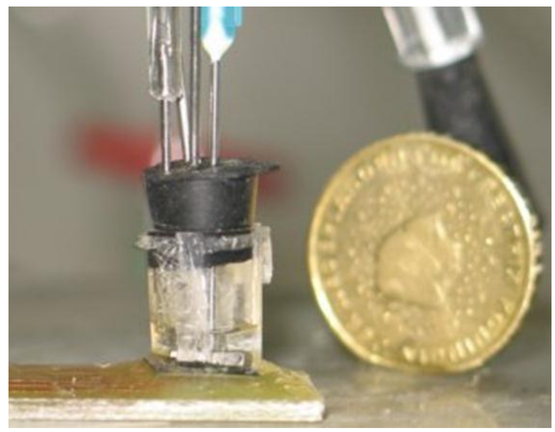

Figure 1.2 Prototype microbioreactor with 100 μl working volume developed in the BIOS/Lab-on-a-Chip group

1.2 Problem statement

On line measurements and process automation is a necessity for microbioreactor operation. In microbioreactor operation, often sensors and actuators from the microbioreactor system are connected to a data acquisition device for in- and output of signal during a standard process control routine. The monitoring and process control tasks in microbioreactor are normally complex as it involves more than one feedback control looping. As reported by Szita N *el. al* (2005), data such as temperature, dissolved oxygen, agitation, pH and optical density are typically the measured and controlled variables in microbioreactor operation. Due to limited knowledge on computer programming, microbioreactor operators (mostly Biochemical Engineers) would go for a readily available data acquisition device to execute the above mentioned tasks. One of the most widely utilized data acquisition devices is the DAQ produced from National Instruments (NI). As example, NI USB 6343 consisting of 16 number of analog input, 4 number of analog output, and 48 number of digital input/output with 500 kS/s sampling rate. Despite these distinctive features which obviously can be beneficial for process automation of microbioreactor operation, there are relatively expensive compared to a standard microcontroller platform.

Microcontroller based DAQ could be of great replacement to typical DAQ at much lower cost, provided that some of the convenient and features must be given up. For example, most of microbioreactor operations are relatively slow and take long time to respond, thus paying extra money for DAQ to have a very high sampling time isn’t necessary. Microbioreactor would work perfectly with low sampling time without the risk of any loses in terms of the performance and the controlling ability. Any typical microcontroller consists of many digital and analog pins. For example, Mega 2567 consists of 16 analog pins, and 15 PWM pins that can be used as analog outputs and 54 pins of digital input/output. When paired with LabView, Mega 2567 can achieve sampling rate up to 125 S/s.

1.3 Project objectives

The main objective of this project is to design a low-cost microcontroller based platform as data acquisition device for microbioreactor operations.

1.4 Scope of the project

The scope of this project is divided into three main categories. There are as follows:-

a) Microbioreactor design
   - (i) A simple polymer based microbioreactor design that is cylindrical in shape will be used.
   - (ii) Working volume of the microbioreactor is 600microliter.
   - (iii) The microbioreactor should be integrated with suitable temperature and agitation (via magnetic stirrer bar) features.
   - (iv) PT100 temperature sensor will be used for temperature measurement of the microbioreactor content.
   - (v) A hall-effect magnetic sensor will be used to measure the rotational speed of a DC motor used for the agitation control.
   - (vi) The performance of the temperature and the agitation control will be evaluated based on the controller accuracy, response time, and settling time through the set-point tracking experiments.
   - (vii) A Proportional-Integral-Derivative (PID) control algorithm will be implemented for the temperature and the agitation control.
   - (viii) Data on the performance of the temperature and the agitation control of the microbioreactor will be collected and discussed.

b) Microcontroller platform

  i) Arduino based microcontroller will be used as data acquisition card and it should handle the controlling, monitoring and data logging.

  ii) Another dedicated microcontroller will be used mainly to handle the speed measurement and to convert rpm measurements into voltage levels to be read by the Arduino microcontroller

c) Programming for control routines and data logging

  i) Programs for control routines and data logging of the microbioreactor operation will be written by using the GUI LabVIEW^{TM} (National Instruments, US) software.

  ii) The programs will be implemented by interfacing the microcontroller platform with the microbioreactor system.

1.5 Summary of the chapter

In this chapter, brief introduction to bioreactor and microbioreactor been presented. Next, the problem that still exists with the previously proposed designs in the literature been highlighted. Finally, the steps and measurements taken to overcome them and they are all presented as scope of this project.

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