Portable PCR Machine

Hershel Rege, Nathan Franczyk, Yihao Yang

TA: John Capozzo

Introduction

<u>Objective:</u>

Conventional methods for PCR (polymerase chain reactions) are time-consuming and costly with no room for mobility in the design of current machines. Contemporary state-of-the-art machines require, on average, 2-3 hours to perform the PCR process [1] and range from $2,000 - $10,000 to purchase [2]. As a result, this delay in operation can cause widespread inefficiencies for the different types of hospitals, companies, and members of the medical community that use PCR machines [3]. Typical machines also weigh upwards of 50 pounds, rendering them immobile and confined to laboratory space.

Our proposed solution is to develop a portable PCR machine that performs PCR in under 30 minutes, while maintaining a production cost below $500. This machine will weigh under 20 pounds, providing a significant improvement over existing machines. This new portable PCR machine will also be scalable in functionality, able to perform PCR for 2 samples simultaneously with additional installable support for up to 8 samples.

<u>Background:</u>

Polymerase chain reaction is a biological process used to replicate DNA across several orders of magnitude by thermally cycling the reactants until the target amount of replication is achieved. PCR is used in many different clinical areas, including: DNA profiling for forensic science, detection of pathogens for diagnosis of infectious diseases, such as HIV and tuberculosis, early diagnosis of cancerous diseases such as leukemia, and functional analysis of genes [5].

All of these areas are incredibly important to promoting progress in scientific discovery and developing treatments and diagnostics for different diseases. Our new design for a portable PCR machine will lead to faster genetic tests, ultimately saving lives by providing doctors and medical experts the information they require at a faster rate. Portable PCR machines allow field tests to occur, so patients aren't required to wait for their test results to come back from a lab. Instead, through our system, tests can be run in any desired location, leading to faster diagnoses and improving access to this equipment for medical professionals everywhere.

Existing PCR machines are distributed by a variety of companies, including Bio-Rad, Thermo-Fisher, and LabX. However, these contemporary machines still operate slowly, with a average heating rate of 3.3 degrees/second [2]. Additionally, the weight and physical profiles of these machines restricts them from being used in any field testing. Reducing the cost of PCR machines will also make the technology more readily available for certain hospitals and medical companies that require use of these devices, especially in developing countries where the infrastructure is not stable enough for expensive, unwieldy machines [4].

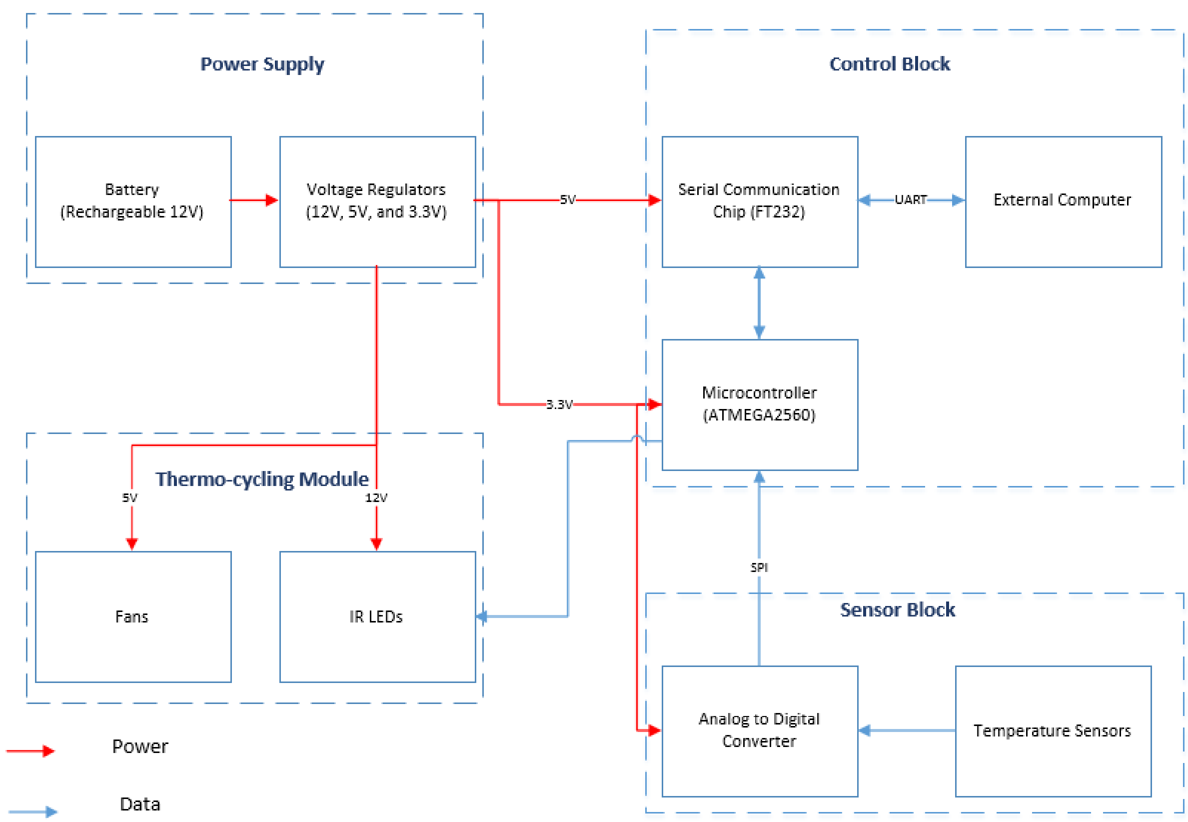
High-Level Requirements:

The portable PCR machine must:

1) Weigh under 20 pounds to maintain portability of the system and be less than 30cm x 40cm x 30cm, which allows it to fit into an average sized back pack [6].
2) Since standard PCR process takes 30 cycles to provide desirable quantities of DNA, our device needs to autonomously perform 30 thermal cycles for at least 2 samples simultaneously without losing power.
3) To meet our intended ramp rate requirement of 5 degrees per second, our machine must be able to observe every degree change. Therefore, our thermal sensor must give a measurement every 0.2 seconds

Design

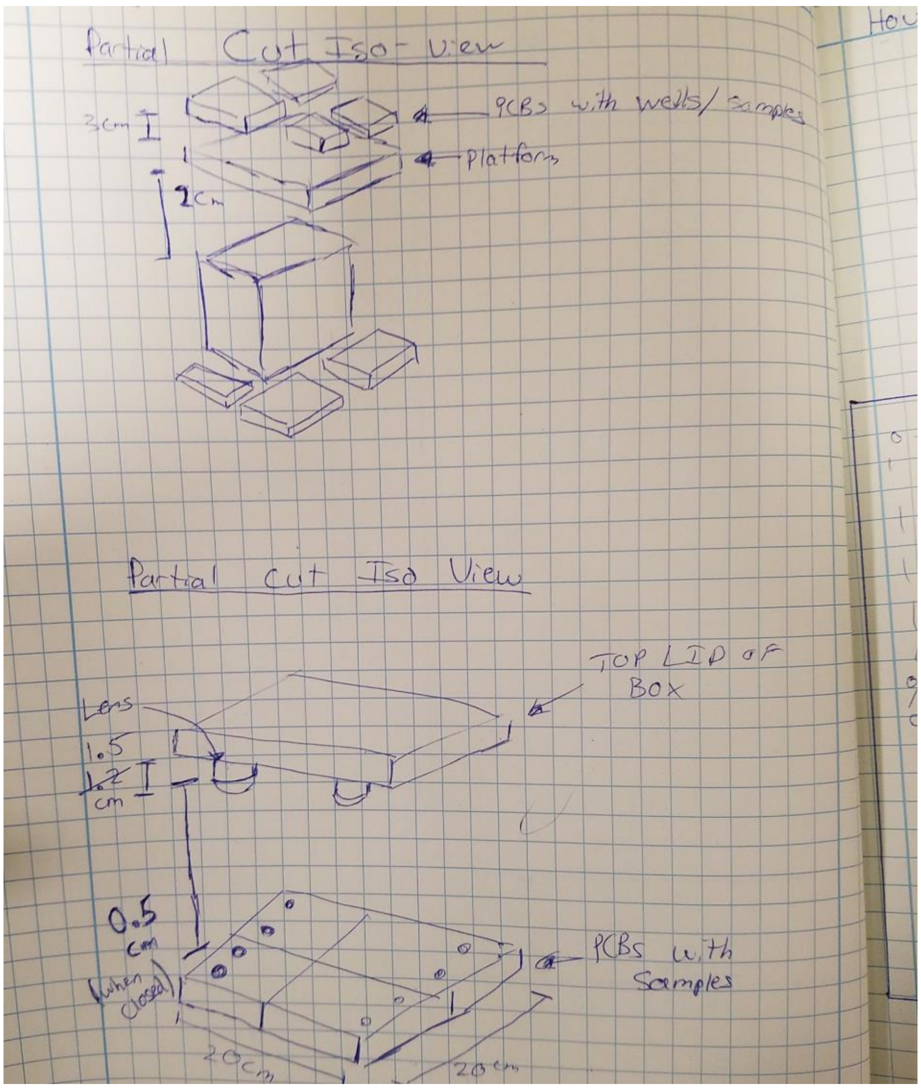
Block Diagram



The power system, defined by the battery and voltage regulator blocks, will power the system and allow for full usage of the portable PCR machine without losing power. The thermal cycling will be directly controlled by the Thermo-cycling Module, using the IR LEDs, fans and instructions from the microcontroller in the control block. The control block will also allow for real-time serial communication, providing information from the Sensor Block about the thermal cycling and transmitting that information to the accompanying external computer.

Physical Design

The most important physical design characteristics involve placement of sensors and high-power components. Specifically, the voltage regulators must be placed far away from the sensitive active components, such as the temperature sensors, to prevent signal noise. Furthermore, the voltage regulators produce a lot of heat that can interfere with temperature control. Additionally, the battery must be kept in a separate area from the main system, to remove the possibility of battery acid leaks onto the physical system.



Functional Overview

1.0 Power Supply
The power supply is used to provide power to all components within the system. The power supply consists of a rechargeable battery and voltage regulators, which step down the voltage to different levels for the different power requirements of the various components in the system. As stated earlier, the design must be scalable, so requirements were calculated to accommodate a maximum of 8 samples.

1.1 Battery
The battery must be able to keep the entire system continuously powered for 30 thermal cycles and maintain a safe discharge rate.

Requirement: The battery must be able to supply 45W and have a capacity of at least 3 amp hours.

1.2 Voltage Regulators
The voltage regulators must be able to step down the voltage to a continuous level, either at 12V, 5V, or 3.3V. They must also be able to handle peak input voltage and current from the battery. They connect directly to the battery and must be kept physically separated from sensitive components.

Requirement: The voltage regulators must be able to maintain the desired voltages of 12V, 5V, and 3.3V for the entirety of the 30 cycles. Voltage must not fluctuate more than +/-10%.

2.0 Thermo-Cycling Module
The Thermo-Cycling Module is used to perform the physical thermal cycling of the samples within the system. The Module consists of IR LEDs and fans, and is externally controlled by the Control Unit.

2.1 IR LEDs
The IR LEDs are used to heat the samples used in PCR. They are controlled by the microcontroller.

Requirement: The IR LEDs must operate at a wavelength of 850nm +/- 43nm.

2.2 Fans
The miniature fans are used to cool the samples.

Requirement: The fans must operate at 3.3V and cool the samples 3 degrees/second.

3.0 Control Unit
The Control Unit manages data transmission between all components of the system as well as maintaining the autonomy of the entire system. The microcontroller directs the Thermal Cycling

Module and provides feedback to the external computer through a serial transmission chip (FT232).

3.1 Microcontroller
The microcontroller, chosen to be an ATMega 2560 due to its scalability, controls the thermal cycling timing as well as the data processing of the sensor measurements. The microcontroller communicates to the Analog-to-digital converter through SPI (Serial Peripheral Interface), and sends serial data to the FT232.

Requirement: The microcontroller must be able to be programmed using Arduino, drive the LEDs and fans used for thermocycling, and must use either 3.3 V or 5 V input. This chip should use less than 5W of power.

3.2 FT232
The FT232 IC is used to send serial data bidirectionally between the external computer and the microcontroller.

Requirement: The FT232 must be able to transfer data at a speed of at least 9600 bits/second.

3.3 External Computer
The computer is used to upload the initial program to the control unit, and to receive the real-time sensor measurements. The computer connects to the system through USB.

Requirement: Computer must be able to communicate serially through USB connection and run Python, LabVIEW, and Arduino.

4.0 Sensor Block
The Sensor Block is used to measure temperature of the samples and transmit that data to the control unit. The information gathered by the temperature sensors is measured using analog devices and converted using an Analog-to-digital converter, which transmits the data directly to the microcontroller.

4.1 Analog-to-digital converter (ADC)
The ADC is used to read analog measurements from the temperature sensors and has a 24-bit resolution to account for even the smallest temperature changes. The ADC connects to the microcontroller.

Requirement: The ADC must be able to detect a change of .2 degrees Celsius when using an appropriate temperature sensor.

4.2 Temperature Sensors
The temperature sensors measure the temperature of the samples.

Requirement: The temperature sensors must be accurate to within 0.2 degrees Celsius.

Risk Analysis

The temperature sensors are a significant risk because the temperature requirement for thermal cycling in PCR is strict (i.e. 75 to 95 degrees Celsius for heating and 95 to 75 degrees Celsius for cooling). Thus, the sensitivity of our sensors will play a crucial role for the success of the system. In this case, the temperature sensors must be accurate to within 0.2 degrees Celsius, however, the accuracy of temperature sensors in general are limited. The potential for system error of more than 1 degree Celsius is possible when using devices such as thermocouples. Therefore, we must ensure that our sensors provide consistently accurate measurements.

Ethics and Safety

Since this project involves building a device that will be used in the medical community and we will disclose all information regarding the product and its intended usage. According to IEEE Code of Ethics #1, if we discover the product does not function as intended, we will act accordingly to fix the issue [3].

According to IEEE Code of Ethics #2, 4, and 8, we will be unbiased in the marketing of our product. We will "treat fairly all persons and to not engage in acts of discrimination based on race, religion, gender, disability, age, national origin, sexual orientation, gender identity, or gender expression."

In order to make our device reliable and marketable, we will be honest and realistic in stating claims and estimates based on available data as following IEEE Code of Ethics #3.

Because this project focuses on developing new technology for the medical space, there are several innovative methods that are a part of the development process. The desired application for this product is for trained members of the medical community to be able to accurately and efficiently test different genetic samples for traces of disease or mutation. Unfortunately, when dealing with biological products, there is always the potential for the product to be used for malicious purposes. Specifically, the genetic amplification that occurs through PCR could potentially result in the amplification of diseased or mutated genes that are harmful to society. According to IEEE Code of Ethics #5, we aim to promote the development of this new technology but we understand that these potential consequences exist, and we aim to mitigate these potential risks by informing the intended users of the correct application of the product.

In correspondence to IEEE Code of Ethics #6 and 7, our product implements the research of the Weizmann Research Group, a renowned biology research group, who are the owners of the underlying technology used in the PCR machine. We will encourage experts to offer feedback of our product and how to improve it further.

Since PCR is a technique used in molecular biology, our project involves the process Users of the product must collect and dispose the samples, so we will take responsibility in making decisions consistent with safety, health, and welfare of the public. More specifically, medical contamination and battery leakage have to be avoided in the whole process. This follows IEEE Code of Ethics #9.

We promise to promote professional development of colleagues and co-workers in their professional development and to support them in following this code of ethics.

References

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