Capstone Report Project NoScope

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Computational 3D Microscope

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This **Masters Project Paper** fulfills the Master of Engineering degree requirement.

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ABSTRACT

This project report covers the development of a computational 3D microscope, NoScope. Using tomographic and light field algorithms, we present a method to reconstruct 3D volumes of microscopic samples taken with a lensless sensor. Business and intellectual property strategies for commercializing NoScope are detailed in the first three sections. The remaining sections highlight the project's technical accomplishments and methods.

Capstone Report
Project NoScope

Ryan Frazier

A paper submitted in partial fulfillment of the
University of California, Berkeley
requirements of the degree of
Master of Engineering
in
Electrical Engineering and Computer Science

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Part I

Problem Statement

1 Project Introduction

As technology has advanced with the emergence of digital computing and signal processing, computers that used to take up entire rooms now fit in a backpack, and doctors and nurses have diagnosis equipment built into their cellphones. However, the optical microscope, a piece of equipment crucial for any medical or experimental lab, has remained unchanged for nearly three hundred years. Modern commercial microscopes rely on fragile lenses and precise alignments, and without additional equipment have no means of sharing the acquired images. Heavy and bulky, they are living fossils in a portable world and would benefit greatly from a technological overhaul.

Many fatal diseases, such as malaria, are endemic in tropical areas around the world. In order to better cure people with such diseases, a faster and more affordable detection and diagnosis method is greatly needed in those region. Traditional microscopes had reached their ceiling of being portable due to its fragile nature, and thus cannot be used as a means to diagnose diseases in the field. A more portable device is needed for doctors and nurses working in those area. With a faster diagnose method, millions of lives will be saved every year.

Imagine a world in which the advantages of microscopy are readily available to every individual with a need due to a low price and viability in a wide range of environments. Furthermore, the microscopic images may easily be made digital. Has a boy in a small African village contracted malaria? How can a doctor in a distant area assess over the Internet a patient's health whose disease requires microscopy? These questions find an answer in a robust, inexpensive, and yet powerful digital microscope. Additionally, people everywhere would be free to explore an exciting and useful unseen world.

How can we achieve our vision then? The clue lies in the advent of digitization and higher computational power; we believe these two factors should be the driving force in future of microscopy. Unlike traditional optics, constrained by the limits of the physical world, computational microscopy can ride the tide of improving electronics, compensating for lack of expensive optics with more complex, but more cheaply achievable computations. In particular, the availability of memory and modern processing speed on common consumer devices opens up access to image-processing algorithms that were previously privy to only the world of laboratory work.

As such, our team wishes to leverage the broader trend of digitization to develop a robust, cheap, portable diagnostic tool that can produce digital images of traditional medical samples. With its advanced computational imaging processing technologies, the NoScope manages to create high-resolution digital images without optical lenses. Abandoning the expensive and fragile lenses, NoScope successfully eliminates the high cost and special handle requirement associated with lenses. In addition, since samples are imaged by USB cameras, the digital files can be shared among individuals easily.

Part II

Capstone Strategy

Contents

1 Introduction

By the end of April 2015, the goal of Team NoScope is to produce a minimum viable product of a prototype microscope that creates three-dimensional images of microscopic samples. We plan on accomplishing this through a series of computational algorithms combining principles of limited angle tomography (Kak et al., 1988) and light field imaging (Levoy et al., 1996). Using these imaging techniques, our hardware will create a three-dimensional image from a series of two-dimensional ones. The goal of this paper is to give the reader a brief introduction to our product, then explain its necessity in the market through its key value propositions, and finally elucidate our strategy for entering the congested microscopy market.

1.1 Our Product

The end goal of project NoScope is a fully functioning, robust microscope prototype that can be taken to market as a minimum viable product. The main factors driving our hardware development are portability, durability, and low cost. In order to limit cost, our team has developed a lensless system that bypasses the need for expensive and fragile lenses, which builds upon the LED array illumination technique in Waller Lab (Tian et al., 2014). We have also incorporated a simple microcontroller on the device, allowing the intensive computations to easily be performed by an attached computer. This significantly reduces the number and complexity of parts, when compared to a traditional microscope.

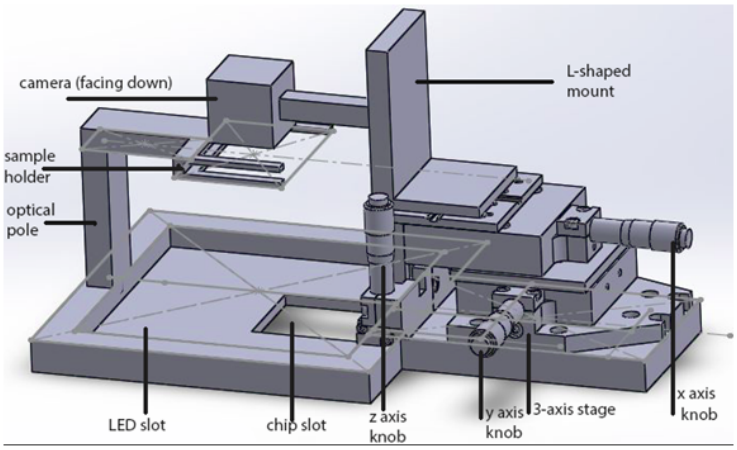

Figure 2.1: Isometric view (CAD) of NoScope.

The current iteration of NoScope consists of a 32x32 matrix of LED's, a camera sensor, and a microcontroller that synchronously triggers specific LED's with camera exposures. During prototyping a custom designed, 3D printed case will house the components. By connecting to a laptop and running software we are developing in parallel with the hardware, the end user will be able place samples on a standard microscope slide and acquire high-resolution 3D images. The inclusion of light field algorithms allows the image to be refocused in post-processing so that various depths of the image can be analyzed by the end user.

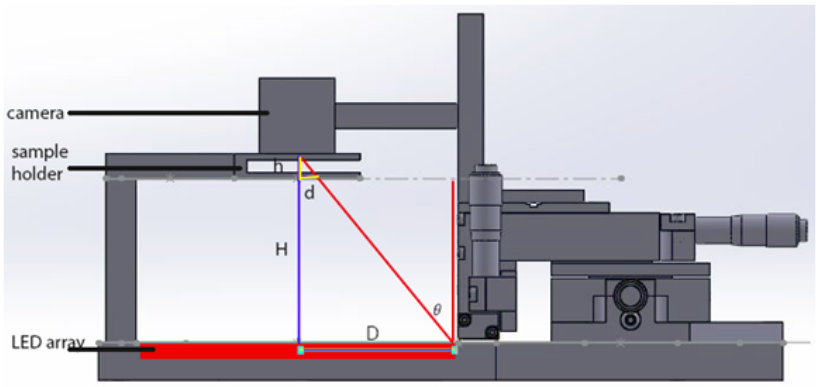

Figure 2.2: Side view hardware schematics of NoScope. Notice the distance of the sample holder to the camera.

Note that figure 2.2 shows the sample placed extremely close (approximately 2mm) away from the camera sensor. This configuration hints at the fundamental working principle of NoScope: casting a shadow of the sample on the sensor. By illuminating a translucent sample, we project an image of the sample on the sensor. Since modern sensors have extremely small pixel pitches (distance between pixel), we are effectively able to view images of its shadow at microscopic scale, thus acting as a microscope. For example, our sensor has a pitch of 5.3μm.

In addition, we are able to generate different 'views' of the sample by illuminating different LEDs. Since each of the LEDs are placed at a different angle incident to the sample, lighting different LED, and taking separate exposures is analogous to viewing an object at different angles. This also forms the basis for digital refocusing.

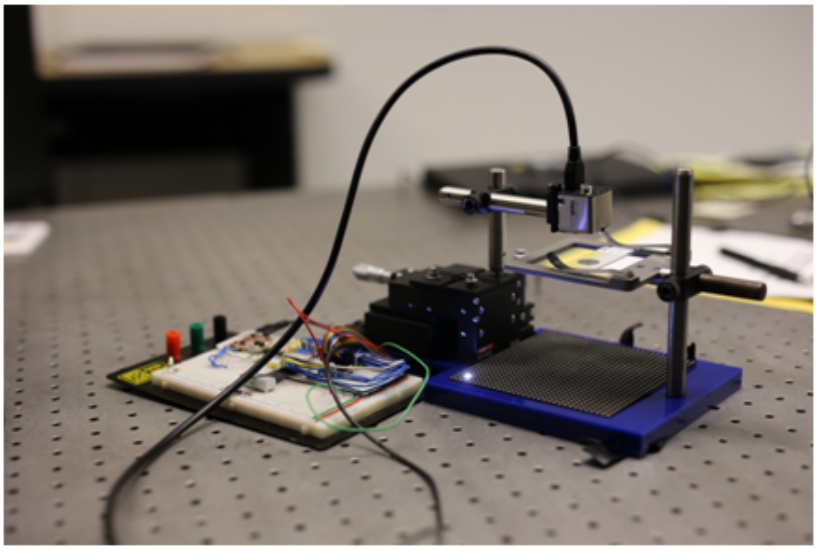

Figure 2.3: First iteration of NoScope. The breadboard is a temporary module and not an actual part of the prototype.

For the current iteration of NoScope, we were able to achieve a resolution of about 32 lp/mm, as well as resolve 3D structures of various microscopic specimens using light field methods. More details can be found in the technical contribution section.

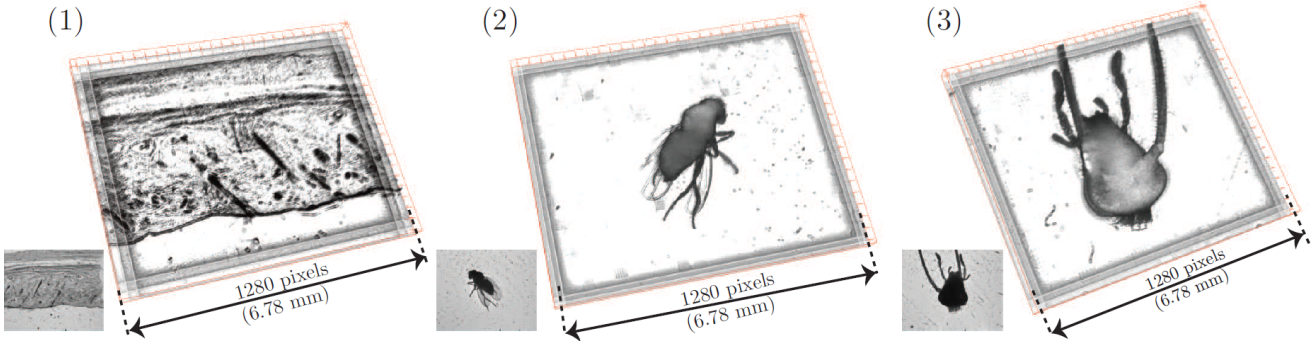

Figure 2.4: Examples of 3D samples from Light field algorithm. No thresholding/post-processing applied. Taken from light field technical contribution report (Lee, 2015).

While the current resolution we can achieve with NoScope is still slightly low, the resolving power of a lensless microscope can be improved by using a sensor with smaller pixel pitch, and better algorithms to account for wave effects. We envision future iterations of NoScope to be used for diagnosing diseases as well as for academic use in teaching environments. In addition, our product can also potentially replace pricey optical microscopes as an inexpensive alternative.

2 Need for Product

Commercialization of NoScope requires the identification of the customers and a full understanding of their needs. In order to find our potential customers, this section will first examine the broader trends in the microscopy industry, and identify a niche for NoScope. Then it narrows down to a specific primary stakeholder and discusses their potential needs, and how these can be fulfilled by NoScope. It further shows that this potential need has not been fulfilled by other products, by analysing the difference between NoScope and our close competitors. Accurate identification of the customer's needs helps companies to shape strategies and have a better positioning. Therefore, this section lays a concrete foundation for our marketing strategy to be discussed in the subsequent section.

2.1 Motivating Trends

As an intrusive new entry, NoScope expects to assist the technology revolution in microscopy and to fulfill needs for underrepresented customers. This section identifies the motivating trends for our microscope in the general industry and our primary market.

Microscopy is a fast growing industry. The market revenue is expected to double in five years from 3.84 billion in 2014 (IndustryARC 2013, p.11). The growing market along with the unique features of NoScope could lead to future investment in NoScope. In addition, this industry is also experiencing a technological shift. The traditional optical microscopes are gradually losing favors due to the limited resolution (IndustryARC 2013, p.13). NoScope might be able to help optical microscopes to regain popularity. The core technology of NoScope is the 4D light field imaging, which is designed to increase the resolution of the sample images without optical lenses. Once this technology has proven to be applicable, it will be possible for NoScope to lead other optical microscope companies to further increase the resolution of optical microscopes.

Despite the industry's maturity, current microscopy still cannot fulfill all its customers' needs. Aside from the expensive cutting-edge equipment being produced by leading companies in this field, there is a significant need for a low-cost product. One particular example is the use of microscopy in malaria diagnosis. According to World Health Organization (WHO), the funding for malaria control and elimination has reached US 2.7 billion by the end of 2013, a threefold increase since 2005, and this

growth of funding has been greatest in Africa Region (WHO 2014, p.12). However, this funding falls far below the 5.1 billion that is required to achieve global targets for malaria control and elimination (WHO 2014, p.12). Replacing expensive microscopes with NoScope can potentially save thousands of dollars for medical facilities, which allows more funding to be channeled into prevention and treatment of malaria.

2.2 Satisfying Stakeholders in Medical Diagnosis

Moving further along the argument of a potential niche in malaria diagnosis, we have thus identified our primary stakeholders as doctors, or medical technicians in malaria-endemic areas. By the end of 2015, there will be about 1 million community health workers in sub-Saharan Africa, estimated by researchers in Columbia University (Singh et al., 2013). However, doctors and nurses alone are not enough to solve the problem. According to WHO, there were about 207 million cases of malaria in 2012 and an estimated 627,000 deaths (WHO 2014b). In order to contribute to the fight against tropical diseases in under-developed regions, we plan to provide these health workers inexpensive and portable microscopes with strong disease diagnosis ability.

The biggest challenge for us is maintaining a low price point. Governments of developing countries cannot afford sufficient expensive medical equipment to satisfy diagnostic needs. On the other hand, doctors from nonprofit organizations mainly rely on donations from external parties, and also have limited budgets. Therefore, expensive microscopes–which are in the range of thousand dollars–are not suitable for our primary customers.

Our key value proposition is thus to make our hardware highly affordable by using a lensless design. Microscopy lenses are particularly expensive, comprising the majority of a typical microscope's price. Naturally, by avoiding lenses altogether, we can significantly reduce our selling price. This allows our customers to have more money to invest in disease treatment rather than diagnosis.

Our second value proposition is portability and robustness. It is no coincidence that many of the malaria-endemic areas, such as North India, and Africa, are also less economically developed. Consequently, these regions may lack proper transport infrastructures. The conventional microscope lens is a piece of equipment that not only is heavy, but also fragile. As such, these lenses often come with their own protective suitcases. These logistical factors further compound the difficulty of getting

the microscope to the field. By removing the lens entirely, we address the issue of accessibility of microscopic diagnostic services by transforming the microscope into a light, electronic device.

In addition to being lensless, NoScope boasts a unique feature of 3D imaging. The ability to view samples in 3 dimensions can help increase the accuracy of disease diagnosis. Most disease diagnosis relies on morphological discrimination of unhealthy cells based on pathological features (Tadrous, 2011). A 3D image allows doctors to view the sample from different angles, and observe features that might otherwise be hidden in 2D projections or slices. This leads to higher accuracy identification of cell types or parasites. Incidentally, as the following section will show, the 3D imaging feature also distinguishes us from the rest of our competition, making NoScope the most suitable product for disease diagnosis.

2.3 Differentiation: NoScope vs Competitors

In the process of selecting our closest competitors, we have considered the similarity of their technology to ours, as this is a good indication of how directly they compete against NoScope. Building on this, we have further subdivided our competitors coming from the industry and academia. On the commercial side, this section will cover our potential rivals from Lytro, Cellscope, and Pelican. In academia, we will examine the field-portable tomographic microscope by Ozcan Research Group in UCLA.

In comparing our product with those of the competition, we keep in mind the key criteria of cost, portability, and computational imaging capabilities–particularly any 3D capabilities. Although the products of these competitors may hold some advantages over our product in certain areas, NoScope still holds its weight in the market of lightweight, inexpensive imaging systems for disease diagnosis.

Competition in the Industry

In this subsection, we evaluate three industry competitors: Lytro, Cellscope, and Pelican Imaging.

Lytro

We start our industrial competitor analysis from the computational imaging system developed by Lytro. This system is marketed toward everyday users who want to capture depth-related details in their life photos and have more post-processing options available to them to modify these photos. The system boasts a small form factor that makes it convenient to be carried around without hassle. The

light sensor array requires lenses to properly focus the light for capturing light-field information. This light-field technology enables Lytro to vary parameters such as depth-of-field as well as numerical aperture in post-processing (Lytro, 2015), which is a large factor in the appeal of computational imaging systems. However, the method of computational imaging at work in their product does not allow for high-resolution 3D images due to the poor range of angles available to a camera in a macroscopic scene. Most importantly, Lytro does not focus on disease diagnosis and is incapable of microscopy, and thus fills a different need in the imaging market compared with our target customers.

Cellscope

Cellscope offers strictly an optical assembly to accompany a user's smartphone to allow for convenient microscopy while taking advantage of computing power and hardware already in the user's possession. Their product consists of a mount for a smart phone, mirrors and lenses, and a mount for the specimen to be viewed. In concert with a smart phone, this assembly accomplishes the key points of being lightweight and affordable while allowing for taking microscopic images. (Cellscope, 2015) Despite these advantages, Cellscope does not offer computational imaging, and thus has no capability of creating 3D images, which renders it less useful in garnering detailed information about samples, such as malaria parasites.

Pelican Imaging

Pelican Imaging has developed–but has yet to sell or contract out use of–a computational imaging sensor capable of replacing the camera in future smart phone models. The capabilities of a smartphone with this type of integration exhibit much similarity with those of Lytro cameras, particularly post-processing to alter many key characteristics of photos. Hence, we find that Pelican's sensor module matches up against our product in much the same way as Lytro does. However, there is potential for a future product combining Pelican's sensor module as Cellscope to fill the same market need as our product. Such a combination would combine the advantage of 3D imaging with portability and microscopy (Anderson, 2015). However, the optical components present in Cellscope's product may put the price point higher than our product. This combination would also rely on the user to already have a smartphone with Pelican's sensor.

Although this competition in still theoretical at this point, it indicates that there is movement toward filling this niche in the market that we are targeting, and thus informs us to move quickly in developing

our product to gain hold of the market.

Competition in Academia

Field-portable Tomographic Microscope - UCLA

Looking at our academic competitor, Ozcan Research Group in UCLA has a design that bears many similarities to our proposed design. Namely, their microscope employs an LED array, as well as a lensless design, both of which are also key features in our device.

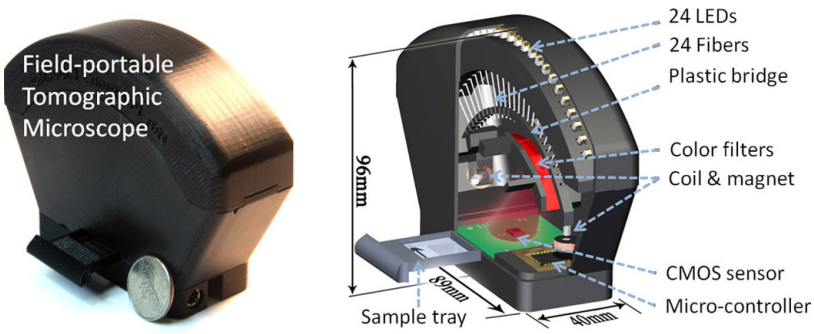

Figure 2.5: The schematics of Ozcan Research Group's tomographic microscope.
[Image Source: `http://www.spie.org/x84293.xml`]

Their image processing technique also resembles ours on the surface. Using multiple angles of illumination, their device takes images of the same specimen at different angles. In addition, in order to extend the angles of illumination beyond one axis, the coil and magnet in the device can electrically actuate the optic fibers to light the sample differently, giving the device an additional axis of data to work with. Following which, the on-board chip on the microscope processes these images into a 3D hologram using the technique of dual-axis tomography (Isikman et al., 2011).

A closer examination reveals several differences between the two devices. In terms of image processing, we are currently tackling the problem using two approaches: 4D light field, as well as 3D tomography. For the more comparable tomography technique, our device differs by virtue of the number of LED axis we have. By employing a full 2D matrix of LEDs, as opposed to just two axes in their device (additional axis by driving coils), our design endows us with multiple axes of data to work with. Consequently, we expect to be able to achieve a higher theoretical fidelity when it comes to reconstructing the 3D structure.

Aside from the algorithm used, we expect our device to be far lower cost than UCLA's microscope, owing to the simplicity of our design. The first reason is that the domed-shaped housing for the LED, which has to be custom made, is much more expensive than a flat piece of LED array we are planning to use, which can be bought off-the-shelf.

Additionally, UCLA's microscope achieves their second axis of illumination by actuating magnetic coils on the device (Isikman et al., 2011). This undeniably adds complexity, and hence cost, to the device. In contrast, as mentioned in the analysis of our tomography algorithm, the nature of our 2D LED array already allows us to have multiple axes of illumination. Taken together, we expect our device to be simpler in design, but still capable of achieving the same, if not better, resolving capability.

From our analysis of competitors above, we find our product provides a service not yet filled by others. Although Lytro, Pelican Imaging, Cellscope and Ozcan's Research group have somewhat similar products, our end goal will serve a need separate from all of them by providing a portable, low-cost microscope capable of 3D imaging focusing on disease diagnosis.

Since we accurately identified the specific need of our stakeholder, we are better able to differentiate ourselves from our competition. As such, we have laid the foundation of a specific need we hope our product will eventually be able to satisfy. The following section will thus use that niche as an anchor to expand on the broader strategy of entering the market.

3 Entering the Market

Successful entrance into our target microscopy market necessitates an overall understanding of the forces and trends permeating this market. In this analysis, we aim to garner insight regarding those technological and business aspects that impact our strategy to enter the market, which include profitability under competitive forces, and the pricing of our product.

3.1 Competitive Forces Analysis

We first seek to gain a thorough understanding of the factors affecting profitability in this market. In evaluating these factors, we apply Michael Porter's well-known framework of the "Five Forces" model to gauge competitive forces. We further consider positioning ourselves according to Clay Christensen's "disruptive innovation" model in order to help combat each of these forces.

As this technology has not yet been commercialized in the application of microscopy, considerable opportunity exists in the market for our product. However, we find the current industry environment hostile to new entrants such as ourselves, and we must overcome strong barriers to entry in order to gain a foothold in the market. Substitutes for our chosen application of malaria diagnosis–medical diagnosis and Rapid Diagnostic Test RDT–pose a threat of luring customers away from our product. Finally, we consider what power buyers and supplier might have over our profitability in this market.

Established Rivals

A small number of large companies command most of the power and profit in the microscopy industry; indeed, more than 90% of revenue in the $5,682 million industry of 2013 went to a limited number of key players (McWilliams, 2013, p. 135). Looking at industry reports, we find that these key players largely consist of glass manufacturers (Uba, 2015, p. 14). The clout of this cluster of glass manufacturers presents a considerable barrier to entry due to the limited number of suppliers. However, since a large advantage of the technology we employ is the lack of optical components such as lenses, we expect to be minimally affected by the clout of this cluster of glass manufacturers. This allows us to circumvent the strong barriers to entry set up by the larger players of the industry.

Established microscope companies have more resources and better reputation than we would upon

entering the market. How then can we penetrate the market to become profitable while minimizing retaliation from incumbents? The answer lies in Clayton Christensen's "disruptive innovation" model. By taking advantage of the un-catered needs of markets with lower gross margins, we can reach a customer base with a smaller budget and thus enter the market (Christensen, 2015, p. 1). The lensless nature of our system brings our costs low enough to be highly competitive, and undercut the cost of microscopes with similar specifications, as we discuss in the next section on pricing. Large microscope companies will run the risk of degrading their profits in order to compete on a similar price point.

Furthermore, our technology presents its own barrier to mimicry. After searching through commercially available options, we found that computational imaging has not yet been commercialized for any microscope, so companies would be forced to conduct R&D in the field of our technology in order to take advantage of the value that saves product cost. Lastly, even if competitors increase the R&D effort for a comparable product, they run the risk of self-competition. The customer bases between our initial customers and a typical microscope producer are not mutually exclusive; these competitors would compete with their own products for the same customers if they chose to mimic our technology.

Buyers and Suppliers

The buyers of microscopes come from various industries. The life science industry is the largest player on the buyer side with 26% of the market, followed by the semiconductor industry, education, and the nanotechnology industry, with market share as shown in Table 1 below (McWilliams, 2013, p. 7).

Table 2.1: Global microscopes market share by major application, 2012 (McWilliams, 2013, p.7).

Industry	**Proportion of Market**
Life science	26%
Semiconductors	24%
Education	12%
Nanotechnology	7%

From Table 1, we can clearly see that the life science industry is the biggest player in the buyer's side, but it does not dominate the market. The semiconductor industry and material science industry both have similar market shares as the life science industry on the buyer side. Furthermore, if we look into

the life science industry, microscopy has been the de facto tool of cell and tissue analysis from 1800 (Rosen, 2005), and it is extremely hard for the industry to find substitutes for the microscope and change its 200 year-old habit. Therefore, we can safely conclude that the buyer power of microscopy industry is relatively weak.

If we look at the components of a microscope, its most expensive and fragile parts are the lenses. Looking at the major supplier microscopes, the optical instrument industry, we find an interesting phenomenon–the major players in the microscopy industry, such as Nikon and Carl Zeiss Ag (McWilliams, 2013, p. 135), also have business in optical instrument manufacturing industry (Oliver, 2015; Uba, 2015). This shows that the suppliers of large microscope companies are themselves; these companies most likely found it profitable to perform backwards integration by bringing manufacturing in-house. The supplier power is thus weak for the large companies in the industry. However, this also means small companies and OEMs in the industry need to buy lens from their major competitors. The supplier power for small companies in the industry is quite high. In order to mitigate the strong supplier power from those big players, we designed our product to be lensless. The electrical components of our product, a LED array and a CCD camera, are easily replaceable. Therefore, we can conclude that the supplier power for our product is also relatively weak.

Threat of Substitutes

Next, we consider the power of substitutes for diagnosis of malaria by evaluating the two major substitutes: clinical diagnosis and Rapid Diagnostic Test (RDT). We show that microscopy remains the de-facto gold standard for diagnosing malaria, and hence, the threat of substitution is weak.

Plasmodium is the malaria-causing parasite. Conventional diagnosis of malaria works by staining a patient's blood smears using a mixture of acidic eosin and methyl blue, known as Giemsa's solution. (Fleischer et al., 2004, p. 2). This solution stains the *Plasmodium* infecting red blood cells, allowing technicians to detect their presence under a microscope.

Unfortunately, the microscope has its limitations; financial and technical obstacles combined preclude microscopy from being more widely used. Current microscopes are inherently bulky and expensive. Furthermore, the typical optical microscope requires a trained technician to operate, increasing the difficulty of getting a good microscopy test in poor rural regions.

In spite of that, medical experts widely consider Giemsa microscopy to be the most reliable method for diagnosis (Murphy et al., 2013, p. 2). This is due to its low per-use cost, at approximately USD $0.12 0.40 per smear (Wongsrichanalai et al., 2007, p. 6), and its ability to quantify accurately, the severity and variant of *Plasmodium* in the blood sample. This is also the reason why we have targeted malaria diagnosis as our initial market; our simpler lensless microscope can increase the accessibility and affordability of good microscopy service in this much needed market.

Clinical Assessment

We now consider the most basic form of diagnosis: clinical assessment by a doctor. The process of clinical diagnosis starts with recording a patient's travel history. More specifically, this considers any high-risk endemic area in a one-year window prior to diagnosis, such as Africa, North Korea, or North India. However, this has the flaw of assuming an accurate travel history. In addition, the highly variable incubation period across *Plasmodium* variants means that, in some cases, even a one year period is not enough to cover all bases. For example, the vivax variant of *Plasmodium* found in North India and Korea will only start attacking the body 12-18 months after the mosquito bite (Griffith et al., 2007).

Moreover, even after establishing the travel history, recognizing malaria infection based purely on symptoms is not straightforward. Early symptoms of malaria bear many similarities to other common diseases, such as fever, chills, headache, and malaise. Inevitably, this complication hampers the early diagnosis of malaria, especially when it is at its most treatable stage. Unfortunately, it is only in the later stages in which the most telling, but fatal, symptoms surface. These includes coma, anaemia, hypoglycaemia, and more (WHO, 2010, p. 4).

Ultimately, diagnosis itself cannot provide confirmation of malaria infection. This implies that most clinical diagnosis will invariably fall back on microscopy as a final step. Naturally, it seems reasonable to deduce that pure clinical diagnosis is a weak substitute for giemsa microscopy.

Rapid Diagnostic Test

The next best alternative is known as Rapid Diagnostic Test (RDT). RDTs are dipsticks which indicates the presence of antigens (proteins) secreted by *Plasmodium* in the blood. A patient uses a RDT by pricking a small amount of blood on a test strip containing antibodies targeting specific *Plasmodium* antigens. Depending on the result, the blood colors the test strip in a specific manner, allowing

a quick diagnosis.

Figure 2.6: Example of a Rapid Diagnostic Test, BinaxNOW from Alere. Source: `https://ensur.invmed.com/ensur/broker/ensurbroker.aspx?code=12000304&cs=26232437`

The advantage of using RDT is that it is fast and easy to use. Unlike a microscope, the small RDT test kit can be brought out to the field, and be used by an untrained person by reading off the strip. It also does not require an electricity source. Most importantly, the RDT can give an indication within 5-20 minutes, making it suitable for screening a larger number of people. This also accounts for its recent popularity. These tests are increasing in popularity and use in recent years, with 319 million units of reported sales in 2013, up from 46 million in 2008 (WHO, 2014, p. 22).

Despite its popularity, RDTs remain far from being a microscopy replacement. The first issue is that RDTs are only sensitive towards one variant of *Plasmodium*, the falciparum. For other variants, the RDT becomes less sensitive, especially when parasite density is low (Wongsrichanalai, 2007). This opens up the danger of false negatives. Second, the RDT is unable to distinguish between variants of *Plasmodium*, which is essential for effective treatment. Third, RDTs cannot quantify the concentration of the parasite in the blood, which indicates the severity of infection.

The limitations of RDT put it, at best, a complementary product, rather than a substitute, for microscopy. It is currently well-suited for giving quick diagnosis in areas where microscopes or technicians are unavailable.

Having considered the available substitutes, we believe NoScope attacks a sweet spot in the space of diagnosis by offering diagnostic reliability, accuracy, ease of use (no optical focusing), and affordability. By carefully segmenting an application of microscopy that has no viable substitutes, we have positioned our lensless microscope in a strategically strong position. As such, a vital specification of our microscope is to be able to resolve the *Plasmodium* variants, as well as doing it affordably, in order to

place ourselves in an advantageous position in the malaria diagnosis market.

Upon examining the competitive forces in our chosen market, we expect to encounter strong barriers to entry. We can circumvent profit loss by taking advantage of the lensless nature of our system. This lack of optical components also contributes to our highly competitive price point, which fuels our use of the disruptive innovation model of entering a market. Large companies ultimately would not provide strong retaliation due to factors of price point, R&D costs, and self-competition. We find buyer power weak due to the large demand for microscope and the unique value of NoScope. Supplier power does not dampen profitability considerably due to the interchangeability of suppliers that our system design affords us. Our affordable and powerful design is highly competitive against the available substitutes. Altogether, we expect these competitive forces to weigh little against our potential profitability.

3.2 Competitive Pricing in a Saturated Market

While the previous section covered the broader business strategy, this section will cover our specific competitive pricing tactics for NoScope. Too low of a price will hurt profits and will not allow us to expand quickly. Too high of a price, however, would put us in direct competition with large microscope producers whose brand recognition and R&D power we cannot match.

The Top-down Approach

To determine the optimum price, we used a top down approach and analyzed Nikon's annual shareholder report. As one of the leading microscope producers, Nikon's 2013 net sales for optical instruments was 41.9 million dollars (Nikon, 2013). At an average cost of $530 per microscope, calculated using `http://amscope.com`'s inventory, this comes to 79,056 units sold per year. Our team wants NoScope to have a 5 year first-generation life cycle with one year of R&D Preceding. Being a smaller startup, our expected sales per year were determined as a fraction of Nikon's annual sales, with expected sales approximately doubling each year as the company grew.

The Bill of Materials for NoScope was calculated using reputable vendors such as DigiKey. This in combination with employee costs was used to calculate annual sunk costs (Figure 2.3). Using this data, we determined that in order to turn a profit on NoScope after three years we would need a product cost of $120.60. Calculating a 50% buffer for unexpected costs leads to a final price tag of $189.99 per unit. This is well below the average traditional microscope cost allowing us to compete with

established rivals price-wise, while still remaining competitive in the event of new market entrants.

Figure 2.7: Accumulated costs vs. units sold for product lifecycle

As mentioned above, we estimate NoScope's Generation 1 Life cycle to last five years. Using the Stages in the Product Life Cycle (Figure 2.4), this would account for our introduction and growth period. While firmware updates will still be pushed through the end of the product's lifecycle, during the last two years, all hardware development will be shifted towards creating a second generation of NoScope.

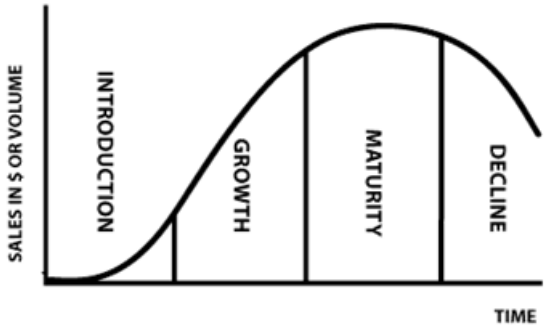

Figure 2.8: Product Life Cycle illustration Source: `https://serrvartisans.files.wordpress.com/2012/03/productlifecycle.gif`

The second generation will be slightly more economical, yet offer more features, such as automatic disease diagnosis and cloud storage services. At this point we will heavily push marketing and brand recognition, having built a stable user base with the first generation model. When NoScope extends from Growth to Maturity, our team will branch off into two distinct consumer products: a medical grade microscope for doctors and other professionals, and a consumer model suitable for schools and

affordable enough to be bought in bulk.

Further on, our company will form an R&D team to research future expansions and applications for our technology. When NoScope enters into the Decline portion of the life cycle, all efforts will be put towards commercializing R&D's prototypes. This may involve changing markets entirely (targeting maker/hobbyist fields instead of medical professionals) and will depend entirely on current market trends. We estimate the total time period from Introduction to Decline to be 10 years, following current market trends as well as the computational "Moore's Law" stating how computing power doubles approximately every 18 months, causing our product to become obsolete if we do not modify it.

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A Return of Investment Calculations

Costs Calculation

	Year 1	Year 2	Year 3	Year 4	Year 5	Year 6
41900000	0	0	7876	23628	55132	118139	236278
Annual Sales:	0	0	0.1	0.3	0.7	1.5	3

Part #	Units per Part	Cost Per Part	Annual Cost	
ATtiny2313	1	0.745	$5,867.58	
HC595 Shift Reg	1	0.1108	$872.65	
LED Matrix	1	50	$393,796.99	
CMOS Camera	1	2.02	$15,909.40	
Camera Module	1	20	$157,518.80	
Housing	1	10	$78,759.40	**$652,724.82**

Part #	Units per Part	Cost Per Part	Annual Cost	
ATtiny2313	1	0.745	$17,602.73	
HC595 Shift Reg	1		$0.00	
LED Matrix	1	50	$1,181,390.98	
CMOS Camera	1	2.02	$47,728.20	
Camera Module	1	20	$472,556.39	
Housing	1	10	$236,278.20	**$1,955,556.48**

Part #	Units per Part	Cost Per Part	Annual Cost	
ATtiny2313	1	0.745	$41,073.03	
HC595 Shift Reg	1		$0.00	
LED Matrix	1	50	$2,756,578.95	
CMOS Camera	1	2.02	$111,365.79	
Camera Module	1	20	$1,102,631.58	
Housing	1	8	$441,052.63	**$4,452,701.97**

Part #	Units per Part	Cost Per Part	Annual Cost	
ATtiny2313	1	0.745	$88,013.63	
HC595 Shift Reg	1		$0.00	
LED Matrix	1	20	$2,362,781.95	
CMOS Camera	1	2.02	$238,640.98	
Camera Module	1	15	$1,772,086.47	
Housing	1	8	$945,112.78	**$5,406,635.81**

Page 1

Costs Calculation

Part #	Units per Part	Cost Per Part	Annual Cost	
ATtiny2313	1	0.745	$176,027.26	
HC595 Shift Reg	1		$0.00	
LED Matrix	1	20	$4,725,563.91	
CMOS Camera	1	2.02	$477,281.95	
Camera Module	1	15	$3,544,172.93	
Housing	1	8	$1,890,225.56	**$10,813,271.62**

Employee Costs	Engineers	Executives	Support Staff	Support Payroll
Year 1	5	0	0	$500,000.00
Year 2	3	2	2	$700,000.00
Year 3	6	2	3	$1,050,000.00
Year 4	6	2	5	$1,150,000.00
Year 5	8	2	7	$1,450,000.00
Year 6	13	2	10	$2,100,000.00

Page 2

ROI

ROI Period (yrs)	3					
Year	1	2	3	4	5	6
Total Costs:	$500,000.00	$1,352,724.82	$3,005,556.48	$5,602,701.97	$6,856,635.81	$12,913,271.62
Product Cost:	**$120.75**					
Product Cost (x1.5)	**$181.12**					

Part III

IP Strategy

1 Introduction

This portion of the report is not meant to be an exhaustive analysis on all possible forms of intellectual property protections. Instead, this is meant to be an extension on our business strategy in the previous section, and a brief outlook on the most pressing IP concerns that may aid or hamper us in NoScope's competitiveness in the microscopy arena.

The most unique and potentially patentable portion of our project is the hardware. Four main pieces comprise our system: the LED array and its controlling system, a sample holder, a camera sensor, and a moving stage to mount the sensor. In particular, it is the specific combination of these components that succinctly captures the three critical value propositions of our project: 3D imaging, lack of lenses, and super-resolution. Light from different, single LEDs will cast shifted images of a specimen directly on our CCD camera sensor, giving us the angular information we need to perform 3D reconstruction of the specimen. In addition, the moving stage allows us to translate the camera sensor in microscopic scales - this creates multiple shifted versions of a single image, allowing us to combine these images using super-resolution techniques to a higher resolution than our physical pixel would allow.

The reasons to focus on hardware patenting over image processing algorithms stem from concerns of practicality. First, most of the algorithms we use are based on already published work, precluding any sort of claim on them. Second, many of our competitors have successfully patented their hardware, and this sets a strong precedence for us to consider following the same route. Moreover, one of our close academic competitors from UCLA, which we have analyzed in the business strategy paper, has successfully patented a utility patent with USTPO.

However, the fact that the UCLA Ozcan group has filed a patent using a technology very similar to ours is also a cause of concern. In the next section, we will examine in detail, their group's patent, and demonstrate that our hardware does not infringe their claim. Finally, after establishing the viability of obtaining a patent, we will explain why team NoScope believes that, although obtaining a patent is crucial for getting the product to market, it will do little to maintain our competitive edge in the long-term.

2 Examining our Competitor's Patent

The name of the patent is "Lens-free wide-field super-resolution imaging device". Its schematic representation of the invention is shown in figure 1 below. In the abstract of the patent, the group describes their design as an imaging system with "an image sensor and a sample holder disposed adjacent to the image sensor" (Ozcan et al, 2014), which bears similarity to our design. Their design also includes "an illumination source configured to scan in two or three dimensions relative to sensor array" (Ozcan et al, 2014), which is also similar to our system. They included LEDs as one type of their illumination sources. In addition, they mentioned in the patent "the system includes least one processor configured to reconstruct an image of sample", similar to NoScope.

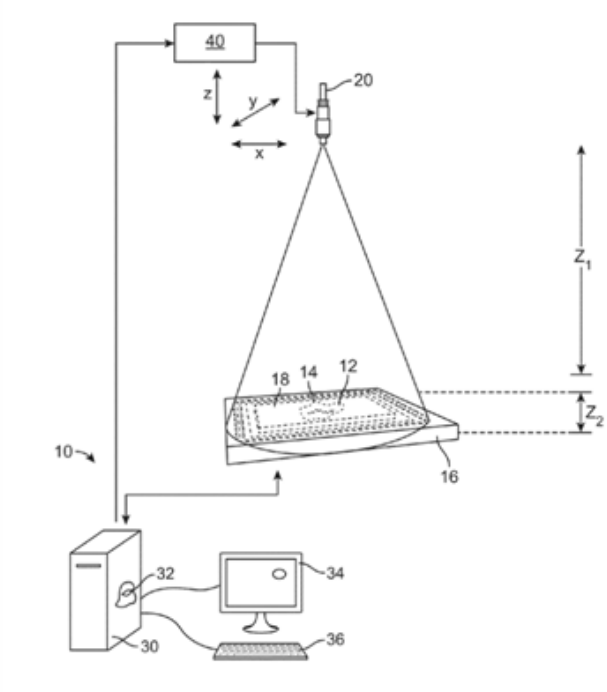

Figure 3.1: Schematic representation of invention of patent filed by Ozcan Research Group (Ozcan 2014, p3)

2.1 Their Five Claims

Although Ozcan's patent has many similarities to our own, there is no possibility of a successful lawsuit on their part due to key distinctions between their patent's claims and our product. Ozcan's patent has 29 claims (Ozcan et al, 2014), which serve to distinguish whether infringement has occurred. Of these 29 claims, there are five main ones with the rest being smaller elaborations to the "big five"

claims, e.g., different light sources or minor changes to the setup. The major claims are diagrammed below.

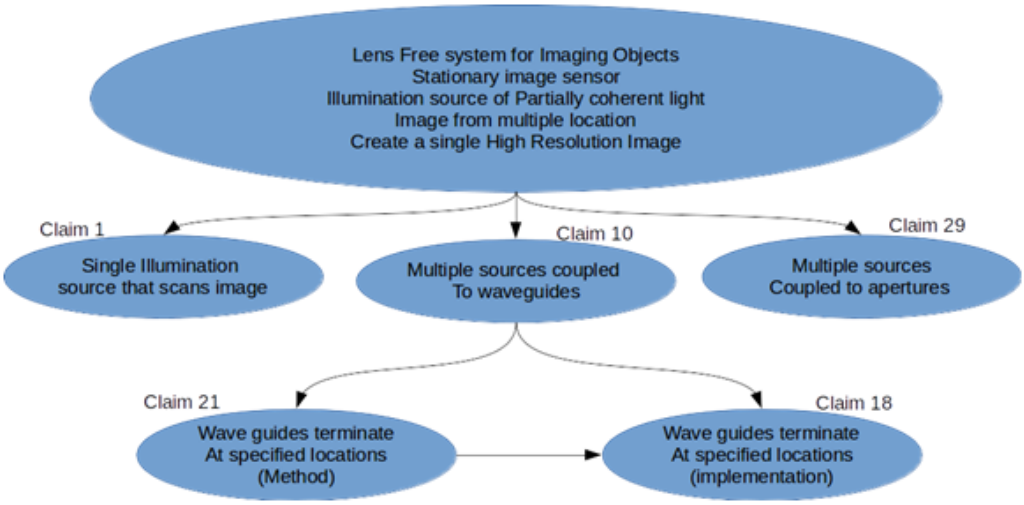

Figure 3.2: Summary of 5 major claims of Ozcan's lens-free microscope.(Ozcan 2014). Arrows connecting claims imply that the claim has all the features of it's parent claim, and additionally it's own sub-features.

To analyze whether our group would be in violation of these claims, each major claim was analyzed using the concept of "Doctrine of Equivalents", articulated in a classic Warner vs. Hilton law case as a test for whether a product violated the claims of a patent (Warner/Hilton, 1997). The Doctrine acts as a three point test. If a product "performs substantially the same function in substantially the same way to obtain the same result," (Warner/Hilton, 1997) it is in violation of the patent's claim. Fortunately for our group, while parts of Ozcan's claims perform substantially the same function in substantially the same way, none of them obtain the same result. Ozcan's patent exclusively covers the creation of a single high-resolution, or "super-resolution" image from a series of lower resolution images. Our group creates a 3D image of the object being imaged, and does not currently make any claims for super-resolution imaging, as we are limited by the resolution of our imaging device. This notable difference would make us exempt from any infringement claims Ozcan's group could make regarding their patent.

3 Competitive Advantage of a Patent

In our previous section, we examined one of our closest academic competitors, Ozcan Group of UCLA, and determined that it is indeed possible for us to file a similar hardware patent that would not infringe on any of their claims. In this section, we will examine the competitive advantages a patent confers in getting our product to market, and finally, make an overall recommendation on devising our intellectual property strategy.

3.1 Differentiation - Hallmark of Innovation

A key advantage of filing for a patent is that it acts as a key differentiating point for our product, especially in a technologically driven industry like microscopy. According to BCC, which performed a filtered search for on USPTO, a large company such as Olympus holds approximately 58 utility patents on optical microscopy (McWilliams 2013: 38). In pitting against ourselves against these large rivals in microscopy, a patent is almost a necessity in signifying technological innovation in our product.

In addition, patents are also vital for the process of raising capital if we were to begin as a startup company. For a startup with focus on selling a hardware device, a patent is not only a direct indication of innovation, it is also the assurance that we hold the legal right to produce and manufacture the product. Conversely, a lack of patent raises doubts from potential angels or venture capitalists looking to invest into NoScope. Obtaining a patent would be an unavoidable requirement if we wish to start a company around our lensless microscope.

3.2 Looking beyond the patent

However, beyond the practical purpose of securing funding and differentiating ourselves from our competitors, a patent will provide negligible long-term competitive advantage in the microscopy market. The first reason is that microscopy is by nature an international market. Filing for patent protection in multiple countries is both time-consuming and expensive. In traditional optical microscopes, the U.S. only accounts for 34% of the overall market (McWilliams 2013: 125). Moreover, as detailed in our strategy section, we are targeting malaria-endemic areas, which includes a considerable number of countries such as North India, and regions in Africa. Unfortunately, IP laws are only applicable in the country in which the patent is filed. Our lensless design will not be protected in our primary geographical market, and the financial resources required for multiple patent filings is prohibitive for

a new entrant like us.

Moreover, unlike what conventional wisdom would suggest, a patent in the microscopy market is unlikely to prevent competitors from producing similar, yet non-infringing designs. For imaging in microscopy, multiple ways of achieving the same function exist, many of which are based on well-established academic work, such as super-resolution. A clear example would be how we ourselves have circumvented UCLA's patent claims with a different illumination device, as well as using a moving sensor stage, in order to achieve similar functions of pixel super-resolution. Thus, it does seem reasonable to deduce that there will likely be potential competitors producing altered designs that can directly compete with NoScope.

Taking into consideration the above drawbacks, our group thus believes that obtaining a patent is a necessary step in order to bring the product to market. While it is necessary for raising capital in the early stages, a patent will not help us establish a monopoly in the malaria niche we segmented. This brings us back to our final point we made in our business strategy paper: a long term sustainable advantage in the microscopy market requires constant innovation, and a continually improving product.

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Part IV

Technical Contributions

• Table of Contents

Introduction

Team NoScope has spent the past seven months developing a lensless, portable 3D microscope to replace traditional microscopes in both general applications and disease diagnose. One of the main advantages of such a system is the elimination of bulky free space optics and lenses in favor of LED light sources and a CCD imaging system. The objective of this paper is to briefly explain the overall development plan, and provide an in depth explanation on NoScope's physical hardware development since the project's conception.

From the start of the project, Team NoScope has been divided into three development subgroups: lightfield image processing, tomographic image processing, and hardware development. Due to the elimination of lenses, extensive image processing is necessary to produce the final 3D figures. The two image processing techniques our team chose to pursue, lightfield and tomography, were picked for the individual advantages each method has. Lightfield processing is noticeably quicker than tomography and allows for artificial depth refocusing after the images have been taken. Tomography, however, is the underlying technology behind CT scanners, and allows a complete 3D image to be created, one that can be dissected and analyzed in layers as opposed to a 3D shell of the observed object. For a broader description of both of these methods, see their respective technical contributions papers (Cui 2015, Hardiman 2015, Lee 2015).

Hardware development was further subdivided into two sections: physical device design and embedded system design. Embedded system design is a crucial part of the overall product and is the focus of this

paper. A well designed embedded control system allows data acquisition to occur as fast as possible, reduces overall cost, and minimizes the image processing time as well as the final image's storage size by manipulating pre-assembled hardware. Later sections explain the complete design process, including constraints, preliminary research, selection of parts, prototyping methods, and final circuit design.

Referenced Literature

Ozcan – *Lens-free optical tomographic microscope*

Before developing the hardware, algorithms, or even general block diagrams, the group first needed to learn about the work already being done in the field. The most influential paper reviewed was written by UCLA Professor Aydogan Ozcan titled “Lens-free optical tomographic microscope with a large imaging volume on a chip. His paper gives an in depth analysis on a system the UCLA group developed for performing lensless tomography. Their setup included a large CCD sensor with a sample placed directly on top of it, and a moving LED illumination sources. The LED would light the sample from various angles, with the resulting shadows cast on the CCD sensor being used to recreate the 3D image (Isikman, et al.). It is from this paper that NoScope's setup takes most of its inspiration. In lieu of a moving light source, however, a 32x32 LED Matrix is used to illuminate the sample. Providing 1024 unique illumination positions at a considerably lower cost.

Adafruit – 32x32 LED Matrix

While the above paper helped determine an illumination source. It provided no information in the way

of how to control the LED matrix. As it is an OEM part purchased through a third party, no formal documentation was available. This is where Adafruit.com's tutorial section for the LED matrix became invaluable. The Adafruit team had gone into extensive detail reverse engineering the matrix. From their documentation we were able to infer the following:

- The matrix is built from a series of LED driver chips acting as current controlled shift registers (Burgess 2015: 37).
- Two rows of the matrix are active at any time (Burgess 2015: 37).
- Up to 64 tricolor LED's can be illuminated at any given time, for a maximum current draw of ~3.84 Amps (assuming chips draw no current and LED's are driven at 20mA).
- A fluid image can be created via multiplexing.
- The Connecting pin header includes 6 RGB color select pins, four address pins, a clock pin, a latch pin, and an active low output enable pin (Burgess 2015: 17).

Adafruit also included wiring diagrams and sample firmware for driving the matrix which aided the group to quickly begin prototyping with the matrix before the embedded system design was complete. However, Adafruit's design is not ideal for NoScope's application. The firmware is very processor intensive, using approximately 75% of the processor's memory, and can only be run on either an AtMega328p or Atmega2560 with an Arduino boot loader installed (Burgess 2015: 5). The custom embedded system improves on Adafruit's because it uses custom firmware and circuitry designed exclusively for NoScope. This frees up substantial amounts of memory and allows the entire system to be run by a smaller and less expensive microcontroller. Additionally, the application-specific firmware

does not multiplex the display, allowing for smaller camera exposures and quicker data acquisition overall. For an in depth explanation of the problem with multiplexed displays, see the appendix.

Atmel – ATTiny2313 Data sheet

Once the ideal microprocessor had been chosen (see the section “Choosing a Microcontroller” for the microprocessor selection process) the provided datasheet was crucial for programming efficiently. Atmel's datasheet for the AtTiny2313 microcontroller provided descriptions of the programming registers, timers, and overall structure of the microcontroller (Atmel Corporation 2010: 7). Additionally, it provided sample code for communication protocols, allowing the microprocessor to “talk” with a computer (Atmel Corporation 2010: 116). The custom system improves on the 2313 design by adding an HC595 shift register as an IO expander. This gives the microcontroller the additional outputs it needs to drive the display for a much lower cost than upgrading to a more power microcontroller with the additional outputs included natively.

Designing the Embedded System

Possible design approaches

When designing an embedded system, there are four main features one needs to consider: cost, speed, architecture, and development time. Power consumption is necessary for low power applications but is unnecessary for NoScope, as it is always plugged into a computer. Architecture (e.g. 8-bit, 32-bit) determines how complex the system is. 8-bit systems run on assembly or embedded-C code and are the

simplest systems with the smallest footprints. 32-bit Systems on the other hand are more akin to miniature computers, and have have fully loaded operating systems installed on them. These are opportune for complex control systems or Digital Signal Processing applications.

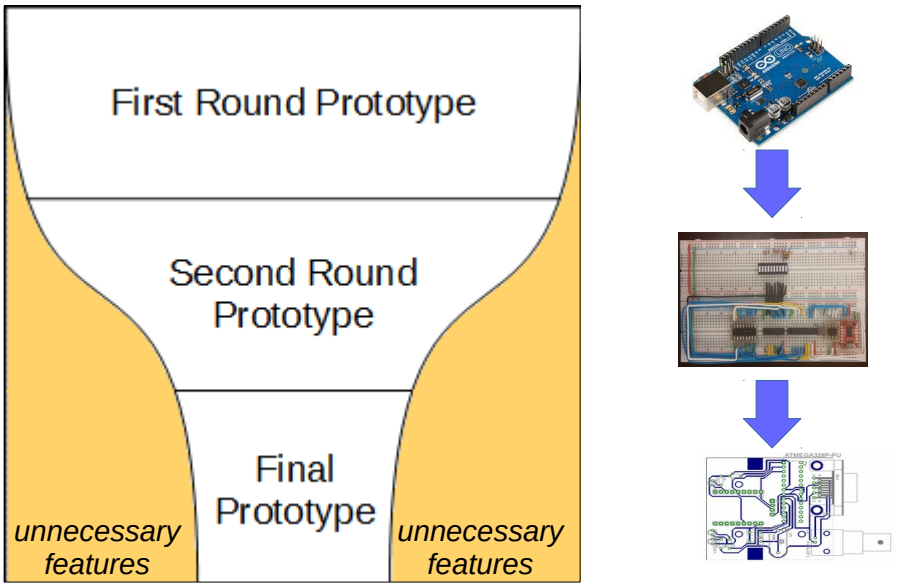

Figure 1: The Embedded system design flow adopted for NoScope. Successive rounds of prototypes eliminate unnecessary features.

The simplest design approach is to leave cost unconstrained and minimize development time. This leads to systems run by powerful microcontrollers and minimal knowledge about the system is necessary, they can be programmed just like a computer would be. NoScope's approach, on the other hand, is a dynamic evolution that sees multiple rounds of prototyping (figure 1). The first round is identical to the "simple method" of minimizing development time to get the system running in as short of a time possible. This is an easy way to examine signals and make sure that the hardware works the way it is expected/supposed to. From there the system is refined into a custom designed circuit build on a proto-board and the final microcontroller is chosen. The firmware is then developed using the

prototyped circuit as a test system, this allows for any hardware design mistakes to be quickly remedied by rewiring the circuit. Finally, once the firmware is running, proving the embedded system layout is accurate, a printed circuit board (PCB) is designed and fabricated. This development approach is far superior to the “Simple approach” described above because it minimizes the end system cost in exchange for a longer development cycle. A pre-built system costs between $30-$50 per system whereas the custom made system is less than five dollars including mass PCB fabrication. Low cost and portability are among the main driving features of NoScope. It's inefficient to have most of the costs tied up in a bloated embedded system when an inexpensive chip could be programmed for a fraction of the price.

Choosing a Microcontroller

A crucial part of Embedded system development is selecting the right microcontroller. An overly complex microcontroller will be more expensive, draw more power, and more often have a large footprint, taking up limited space on a circuit board. Picking too simple a microcrontroller, however, will also set-back development as it may run out of programmable memory, not be fast enough for timing constraints, or lack specific features needed for the application. One should also never choose a microcontroller just because they are familiar with it. And should pick the optimum controller for every application. The steps taken to pick the NoScope's microcontroller, an ATTiny2313, are outlined below.

Diagram the Embedded System

The simplest way to determine what features are necessary for a microcontroller is to diagram the

system as a whole. This can be done either by a block diagram or state chart. For NoScope, both a block diagram and state chart were created. For the block diagram, the microcontroller was the central block with all peripherals extending out from it, this gives an overview of how many Inputs and outputs are needed as well as types of communication protocols that are necessary. The state chart outlines the flow of the embedded system, and is an easy visualization of how complex the program needs to be. Both the block diagram and state chart for NoScope's embedded system can be seen in figures 2 and 3 respectively.

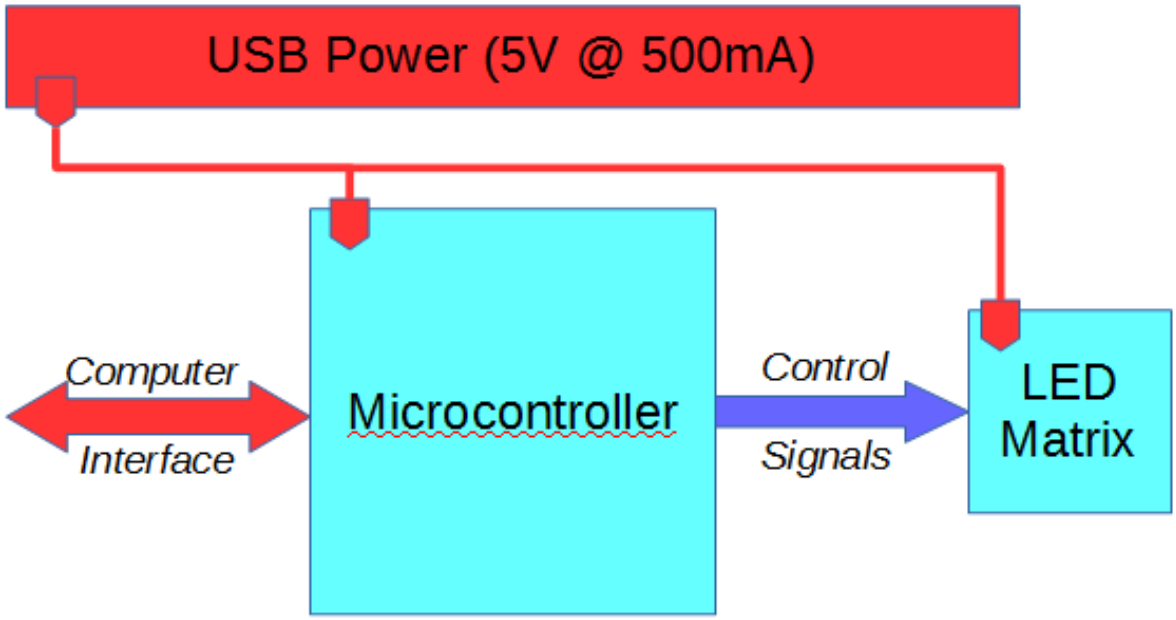

Figure 2: Block Diagram for NoScope's embedded system design

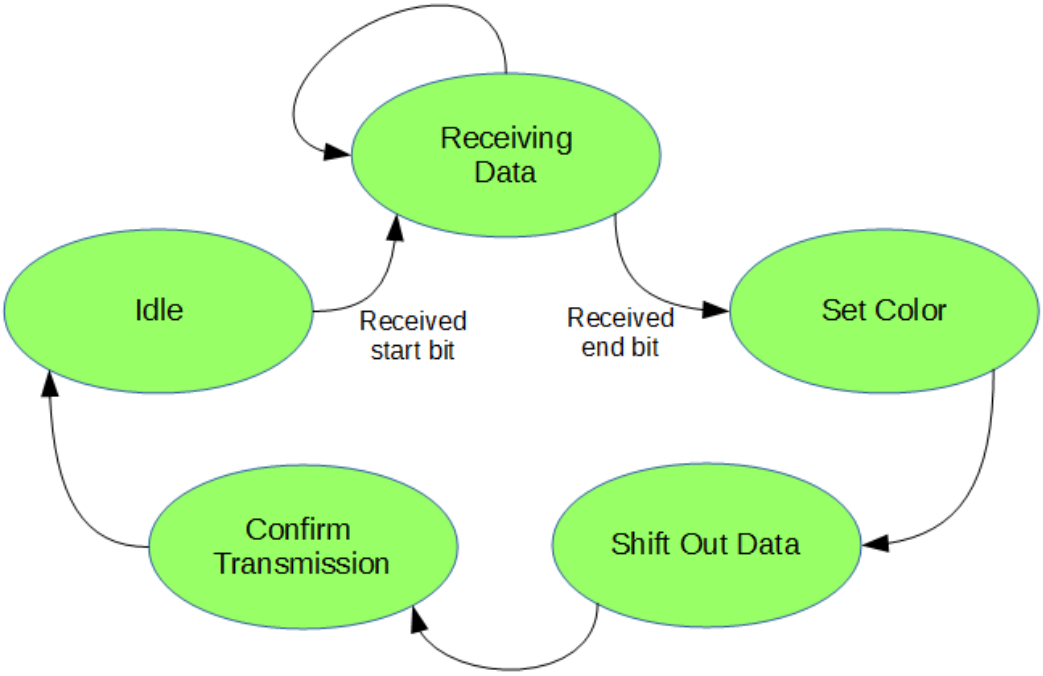

Figure 3: State Machine Diagram for NoScope's Embedded system design

List Necessary Features

From examining the block diagram and state chart it is easy to see which key features are necessary for the microcontroller. The key features for NoScope, as determined by the diagrams are listed below.

- Sixteen data pins
- Two-way communication with a computer
- strict clock rates (>100kHz accuracy)
- software interrupts
- Maximum of 5V operating voltage at <500mA current draw.

Decide on Architecture

From the necessary features, picking the minimum appropriate architecture becomes much simpler. For NoScope the strict clock rates eliminated most 32-bit ARM processors running Linux, as they operate

off of a jiffy-interval of approximately 1 millisecond and would not communicate with the board effectively. Because the system does not execute complex instructions, an 8-bit RISC architecture was chosen as it was the minimum complexity that would satisfy all of our constraints.

Limit by additional constraints

Once the architecture is selected, any additional constraints are applied. NoScope will be produced in large quantities for at least five years, eliminating chips near the end of their phase-out life cycle as well as microcontrollers that cannot be acquired en masse. Microcontrollers that do not comply with RoHS compliance were also eliminated as it limits where NoScope can be sold.

Select Microcontroller

With all the constraints in hand, NoScope's options became limited to a few 8-bit chip families. Ultimately the ATTiny2313 Atmel microcontroller was picked for it's low cost and simple instruction set. The chip runs at an 8MHz clock rate, scalable to 1MHz to conserve power, and has included USART communication to relay data with a computer. The 2kb of memory is sufficient for this specific application, and leaves ~40% of the memory available for further firmware updates.

Results

The Finalized Design

Hardware

The finalized embedded system consists of three parts: an ATTiny2313 microcontroller which controls

all timing and output signals, an HC595 shift register to add output pins to the 2313, and an FT231X USB Serial to USART converter chip. The entire setup fits on a 2 in^2 printed circuit board and is pin accessible for reprogramming the firmware. The sum cost of all the parts is $3.50, approximately a tenth of the cost of an Arduino Mega which would have been used in leiu of the custom designed system.

Firmware

The firmware was coded in C using the avr-gcc tool chain. The firmware monitors the communication line to detect any incoming instructions from the computer. Once it has received a complete instruction set, it light's the appropriate LED on the matrix panel and sends a confirmation character to the computer. This process repeats indefinitely and resets itself on any power faults or detected errors.

Communicating with the Embedded System

To communicate with NoScope, a custom LabVIEW program was written that automates data acquisition. The user can manually program the LED's they want illuminated or upload a CSV file containing the information. Once the program is started, LabVIEW sends the control sequence to NoScope telling it which LED to light as well as what color to light the LED at. The control bits follow the pattern shown in table 1. After successfully lighting the LED, NoScope sends back a confirmation bit (0x21, or ASCII “!”) after which LabVIEW takes an image of the data and saves it according to user specified parameters. Running at 60 samples per second, the embedded system can capture an exposure from every LED in 17 Seconds. Using a non-automated approach, each exposure took ~1 minute, therefore the automated system increases data acquisition by a factor of 3600.

Bit Index	0	1	2	3	4	5	6	7	8
Value	~	R	R	,	C	C	,	c	!

Table 1: Control bit Pattern for communicating with NoScope. RR->Row, CC->Column, c->Color

Contribution towards NoScope's design

It has been repeatedly stated how the custom designed embedded system improves NoScope's design by reducing cost, but it does more than just that. The embedded system increases data acquisition rate considerably, as well as reduces the data size of each exposure (APPENDIX). This allows the lightfield and tomographic image processing to complete faster and with simpler algorithms, further improving NoScope's speed. It also takes up less space, produces less heat, and consumes less power than an off-the-shelf embedded system. NoScope wouldn't be the robust, portable phenomenon it is without a cleverly designed embedded system, and through careful part selection and programming, the 2313 based system is expanding NoScope's potential as an inexpensive, robust microscope substitute.

Part V

Personal Reflections

The embedded system and hardware design has been a constantly changing system the project started last fall. Initially, the team thought it would be possible to design the entire system, image processing and all, on a single device. This would mean NoScope would not plug into a computer, and would have a built in screen and battery letting it stand alone and be truly portable. However, Light field and Tomography are very processor and memory intensive, and without an application specific integrated circuit (ASIC) or programmed FPGA, making the system self-contained would not be feasible. This ended up being an advantage for our team in the long run however, as we learned that one of our largest advantages over a traditional microscope is simply how inexpensive ours is to produce. By allowing the unit to plug into a computer we eliminated over $100 in parts per microscope as well as a drastically shortened our development cycle.

The most important project management takeaway I got from the capstone was that a manager needs to be dynamic with their plans. Road blocks and upsets happen, just like the situation above where a self-contained situation was unfeasible. However, if you are able to roll with the punches and modify your long term goals, a better product than what was initially conceived can come of it. Initial plans are often overzealous as well. Coming in this fall no members of our team had worked on a full year project, and I was the only one with a background in optics. This caused an overly optimistic time line for what we could accomplish in a given period. We didn't account for the fact that this was a new field for many team members, and there would be training times on top of our normal tasks and course load of being a full time student. The GANTT charts were constantly being updated and once we realized what was possible, a more appropriate and realistic time line was created.

Should anybody wish to continue NoScope's work, I would recommend they take the route our group originally thought of, a completely self contained unit. While it would not have been feasible for a first run product, once NoScope gets its foot in the market, a fuller-featured option would be very attractive to universities and professionals who need a truly portable microscope, one that does not need a laptop to view

the data. All of my code, design files, and calculations are well documented, and anybody wishing to pick up where I left off should easily be able to understand the work being done up to this point. I thoroughly enjoyed my time working on the project and with the Master's experience in general. It helped me develop a broader understanding of engineering concepts as well as hone in on specific areas I wanted to study, ultimately enabling me to secure a position as an optical design engineer upon graduation.

Citations

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Appendix

The Problem with Multiplexing for image acquisition

Current displays have more than 6 million addressable pixels, each of which need to update faster than the human eye can detect in order to produce a fluid image. Powering each element simultaneously would require unnecessary amounts of both processing and electrical power to the extent that even an 800x600 pixel display would draw enough current to blow a fuse. To circumvent this problem, a technology known as multiplexing is used. When Multiplexing a screen, only one or two rows are powered on at any given time. These rows receive powered, and then the specific pixels in a row are turned one. The row then loses power and the one following it is turned on. This process repeats in succession and creates what humans perceive as a fluid image through an effect known as persistence of vision. Figure 1 shows an example of display multiplexing through a signal timing diagram for a simple LED display.

The problem with using multiplexing during image acquisition is that the LED's are only on for a fraction of the total time, and a camera exposure is significantly shorter than the period of the display. It is possible for the camera to completely miss an LED and take an image as though the whole display is blank, even though to the naked eye it is on. The only way to solve this without recoding the firmware would be to increase exposure time so that every exposure is observed, or take multiple samples and average them in post-processing. Both of these alternatives reduce NoScope's speed and the ladder adds additional strain to the image processing calculations.

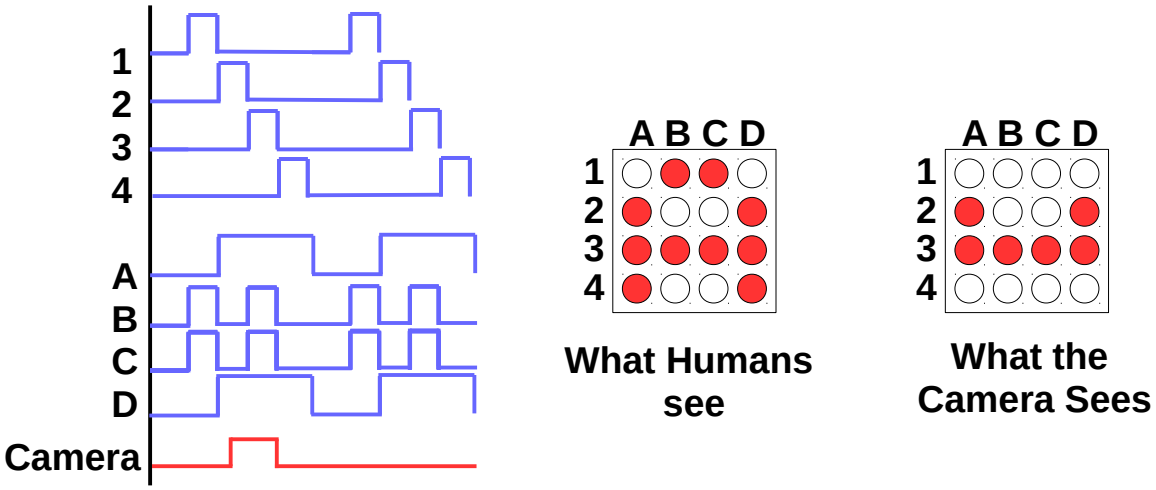

figure 1: Signal timing diagram to reproduce the letter "A" on an LED display using multiplexing. When both signals are high, the LED is lit. notice the Camera image and the human perceived image are not identical due to the camera's short exposure time

ATTiny2313 Firmware

```
//#define F_CPU 1000000UL
#include <avr/io.h>
#include <avr/interrupt.h>
//#include <util/delay.h>
#include "t2313ShiftReg.h"
#include "t2313USART.h"
//Definitions

#define F_CPU 8000000UL // 1 MHz
#include <util/delay.h>

#define pA                      PORTB0 //Address pin A
#define pB                      PORTB1 //Address pin B
#define pC                      PORTB2 //Address pin C
#define pD                      PORTB3 //Address pin D

#define Tx                      PORTD1
#define Rx                      PORTD0
#define CLK                     PORTD2 //LED Matrix Clock Pin
#define LAT                     PORTD3 //LED Matrix Latch Pin
#define OE                      PORTD4 //LED Matrix Output Enable

#define SDI                     PORTB4 //HC595 Serial DataPin
#define SCHP        PORTB5 //HC595 Clock Pin
#define STCP        PORTB6 //HC595 LAT pin

#define RGBRUNS 8
#define LEDRUNS 32

#define T0CAOFLAG 0
#define SRIPFLAG 1
#define RXFLAG 2
#define COLORLOADFLAG 3
#define MATRIXADDRFLAG 4
#define CLEARFLAG 5


//masks
#define RGB2MASK 0xE0 //shift register map first half of RGB Matrix
#define RGB1MASK 0x1C //Shift register mask second half of RGB Matrix
#define OFFMASK 0x00  //MASK to shut off LED's

ISR(TIMER0_COMPA_vect);
ISR(USART_RX_vect);

uint8_t ASCII2num(uint8_t,uint8_t);
uint8_t bitFlip(uint8_t);

void LEDSetColor(uint8_t);
void LEDFillRow();
void LEDShiftOnce();

//uint8_t extractCol(uint8_t *);
//uint8_t extractColor(uint8_t *);

uint8_t HC595Data;
volatile uint8_t USARTData;
uint8_t dataBuffer[9];
uint8_t *DBIndex;
uint8_t row;
uint8_t col;
uint8_t color;


int main(void)
{
          row=0;
          DBIndex=dataBuffer;
          sei();
          USART_Init(0x33); //Initialize USART w/ Baud of 9600
          DDRB|=0x0F; //Set Address ports to output
          DDRD|=(0x01<<CLK | 0x01<<LAT | 0x01<<OE); //SET control signals to output
          LEDSetColor(OFFMASK);
          GPIOR0|=(0x01<<CLEARFLAG);
          while(1)
    {
                    if(GPIOR0&(0x01<<T0CAOFLAG)) //if the timer0 A interrupt set the flag
                    {
                              GPIOR0&=~(0x01<<T0CAOFLAG); //Clear the flag
                    }
                    if((GPIOR0&(0x01<<CLEARFLAG)) && !(GPIOR0&(0x01<<SRIPFLAG)))
                    {
                              GPIOR0&=~(0x01<<CLEARFLAG); //Wipe the flag
                              LEDFillRow();
                    }
                    if(GPIOR0&(0x01<<COLORLOADFLAG))
                    {
                              GPIOR0&=~(0x01<<COLORLOADFLAG);
                              if(row<=16)
                              {
```

```
                                        LEDSetColor(RGB1MASK);
                                }
                                else
                                {
                                        row-=16;
                                        LEDSetColor(RGB2MASK);
                                }
                                while(GPIOR0&(0x01<<SRIPFLAG));
                                GPIOR0|=(0x01<<MATRIXADDRFLAG); //Tell it to load the matrix
                        }
                        if((GPIOR0&(0x01<<MATRIXADDRFLAG)))
                        {
                                PORTD|=(0x01<<OE); //Disable output
                                GPIOR0&=~(0x01<<MATRIXADDRFLAG); //Clear the flag
                                //Set Address Port
                                PORTB&=~(0x0F); //Clear the address pins
                                PORTB|=(16-row); //set the address
                                LEDShiftOnce();
                                LEDSetColor(OFFMASK);
                                while(GPIOR0&(0x01<<SRIPFLAG));
                                for(uint8_t j=1;j<col;j++)
                                {
                                        LEDShiftOnce();
                                }
                                PORTD&=~(0x01<<OE); //reEnable Output
                                UDR=0x21; //Send Confirmation Bit

                        }
                        if(GPIOR0&(0x01<<RXFLAG)) //If something's been received
                        {
                                UCSRB&=~(0x01<<RXCIE); //Disable interrupt temporarily
                                GPIOR0&=~(0x01<<RXFLAG); //Clear the flag
                                *DBIndex=USARTData;
                                DBIndex++; //Increase to the next memory element
                                UDR=*(DBIndex-1); //echo command
                                if(((uint16_t)DBIndex==(uint16_t)&dataBuffer+9) || *(DBIndex-1)==0x21)
                                {
                                        LEDSetColor(OFFMASK);
                                        while(GPIOR0&(0x01<<SRIPFLAG));
                                        LEDFillRow();
                                        DBIndex=dataBuffer; //reset the bufferIndex
                                        row=ASCII2num(dataBuffer[1],dataBuffer[2]); //extract Row Information
                                        col=ASCII2num(dataBuffer[4],dataBuffer[5]); //extract Column Information
                                        GPIOR0|=(0x01<<COLORLOADFLAG);
                                }
                                UCSRB|=(0x01<<RXCIE); //reenable Inturrupts
                        }
        }
        return 0;
}

uint8_t ASCII2num(uint8_t asciiVal10,uint8_t asciiVal1)
{
        uint8_t num10=(asciiVal10&~(0x30));
        num10=(num10<<3)+(num10<<1);
        uint8_t num01=(asciiVal1&~(0x30));
        return (num10+num01);
}
void LEDSetColor(uint8_t Mask)
{
        if(!(GPIOR0&(0x01<<SRIPFLAG)))
        {
                HC595Data=Mask;
            HC595_Initialize(&PORTB,&DDRB,SDI,SCHP,STCP,&HC595Data);
        }
}
void LEDShiftOnce()
{
        PORTD|=(0x01<<CLK);//Toggle Clock
        //_delay_us(1000);
        PORTD&=~(0x01<<CLK);
        PORTD|=(0x01<<LAT); //Toggle Latch
        PORTD&=~(0x01<<LAT);
}
void LEDFillRow()
{
        PORTD|=(0x01<<OE); //Disable output
        for(uint8_t j=0;j<32;j++)
        {
                LEDShiftOnce();
        }

        PORTD&=~(0x01<<OE); //Re-Enable Output
}
uint8_t bitFlip(uint8_t bit)
{
        uint8_t temp;
        for (uint8_t j=0;j<=7;j++)
        {
                temp=(temp<<1); //shift temp towards MSB
                temp|=(bit&0x01); //
                bit=(bit>>1); //shift bit towards LSB
        }
        return temp;
}
```

```
ISR(TIMER0_COMPA_vect)
{
          HC595_Transmit(&PORTB,SDI,SCHP,STCP,&HC595Data); //Transmit the next bit
}
ISR(USART_RX_vect)
{
          GPIOR0|=(0x01<<RXFLAG);
          USARTData=UDR;
}
```