Thesis Proposal

Remotely Controlled Microscope

by

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1. Introduction

1.1. The Goal

The goal of this project is to develop a robust, computer controlled, optical microscope capable of being operated remotely over the internet. The project aims to redesign and expand on a microscope system created by Mr Yilun Fan in 2011 [1]. Specifically, the device will be designed for use in a school environment where it will provide students with additional opportunities to learn how to use a microscope outside of the classroom.

1.2. Relevance

Currently, students do not gain sufficient practical experience with microscopes. This is predominantly because a significant amount of class time allocated to histology is spent explaining background theory. In addition, there is often a limited number of available microscopes shared between many students. One method to remedy this, undertaken at the Rajiv Gandhi University of Health Sciences in Bangalore, was the introduction of virtual microscopy. Students were given CDs with static images of scanned slides and pre-processed sections highlighting important cell structures [2]. While this method was effective at teaching students how to correctly identify microscopic structures, it didn't give them the opportunity to learn how to acquire those images. This project aims to provide a resource capable of teaching students those skills.

Despite development in slide scanning technologies, optical microscope operation skills are still important in medicine today. Slide scanners distributed around the world would allow professionals to diagnose patients remotely, however they are still too prohibitively expensive, particularly for developing countries where they are needed most [3]. Microscopes are cheaper in comparison and, when operated by a skilled technician, would potentially be faster (as a professional would not necessarily need the full picture provided by a scanner if they knew what they were looking for). The microscope system developed in this project will not only develop students' skills with microscopes but also give them an introduction to the growing field of telemedicine.

1.3. Desired Functionality

The microscope skills that a school student is required to have are:

- Slide manipulation
- Focusing the microscope for a range of magnifications
- Using stains to add contrast to particular cell structures

These competencies combined with the goal of the project - to provide a system that is accessible to multiple students outside of the classroom - determined the required functionality of the system:

- Slide translation in the X-Y frame (manipulation)
- Slide translation in the Z frame (focus)
- Adjustable magnification
- Adjustable light source wavelength (within the visible spectrum)
- Automated slide changing
- Interface between the microscope and the internet

The aim of this project is to design a remotely operated microscope system that gives students a chance to learn about the physical operation of a microscope. Because of this the system will be designed for robustness rather than precision and repeatability. For example, rather than specifying coordinates of a feature on a slide that the machine must move to, students will move the platform back and forth until they find what they are looking for. This will more closely replicate how slide manipulation must be done in the laboratory.

2. Background

2.1. Optical Microscopy

There are three main classes of microscope (optical, electron and scanning probe), all of which are used to view objects not visible to the naked eye. This project focuses on the development of a bright field optical microscope. These are optical microscopes which use a condensed light source to illuminate the specimen from underneath. Figure 1 shows a typical modern bright field microscope system.

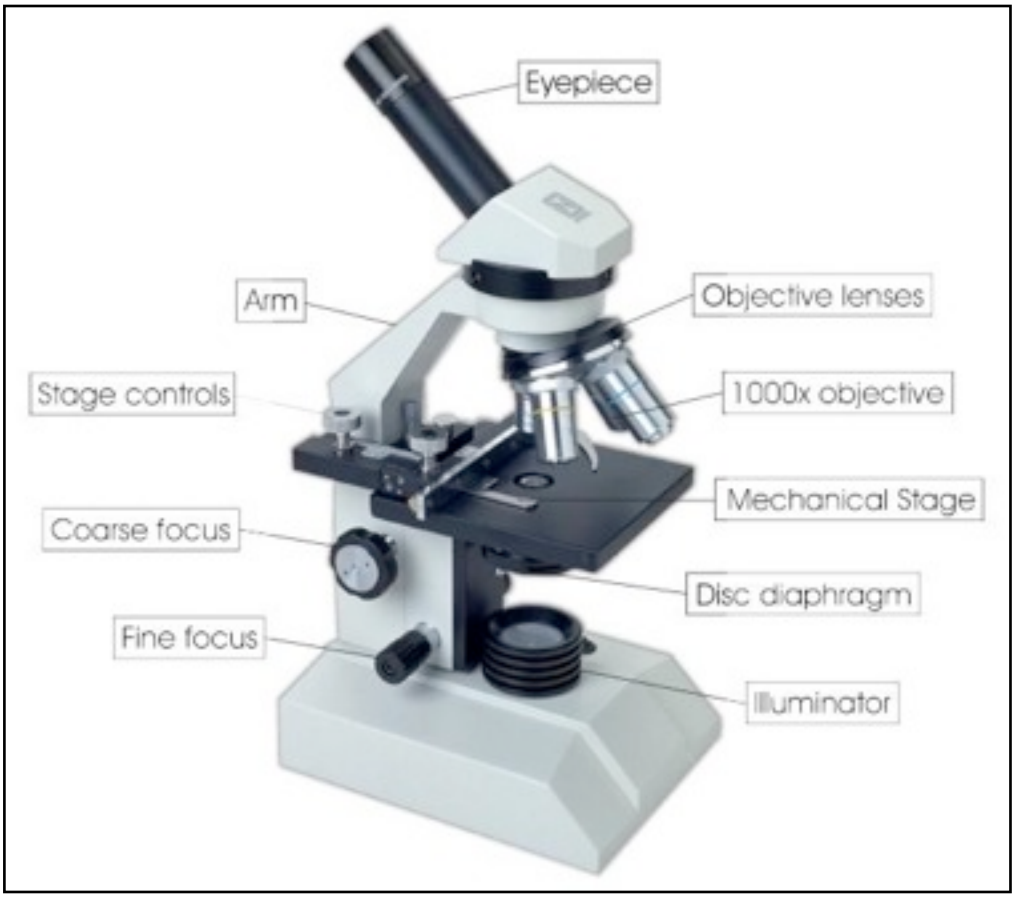


Figure 1: A modern bright field microscope

The microscope has several features to facilitate observation of the various parts of the specimen slide. Because the project aims to mimic the operation of a laboratory microscope all of these features will be included in the user's control interface:

- Stage controls to move the specimen relative to the objective lens
- Multiple magnifications
- A course and fine focus knob
- A disk diaphragm to adjust the level of light reaching the specimen.

The image is often improved by staining, a process which involves adding dyes which bind to certain parts of the specimen. This increases the amount of light absorbed in those parts and hence improves the contrast of the overall specimen [4]. The contrast can be further improved by only illuminating the specimen with wavelengths of light absorbed by the dye. This functionality will be included in the project through the use of a light capable of illuminating at specific wavelengths.

2.2. Prior Art

Two existing designs for a computer controlled microscope were reviewed as well as a virtual microscopy system. A breakdown and analysis of each system was performed in sections 2.2.1 - 2.2.3. A summary of the good and bad aspects of each system can be found in section 2.2.4

2.2.1 Computer Controlled Microscope - Mr Yilun Fan [1]

Mr Yilun Fan's project focused on designing the proof-of-concept, remotely controlled microscope system shown in figure 2.

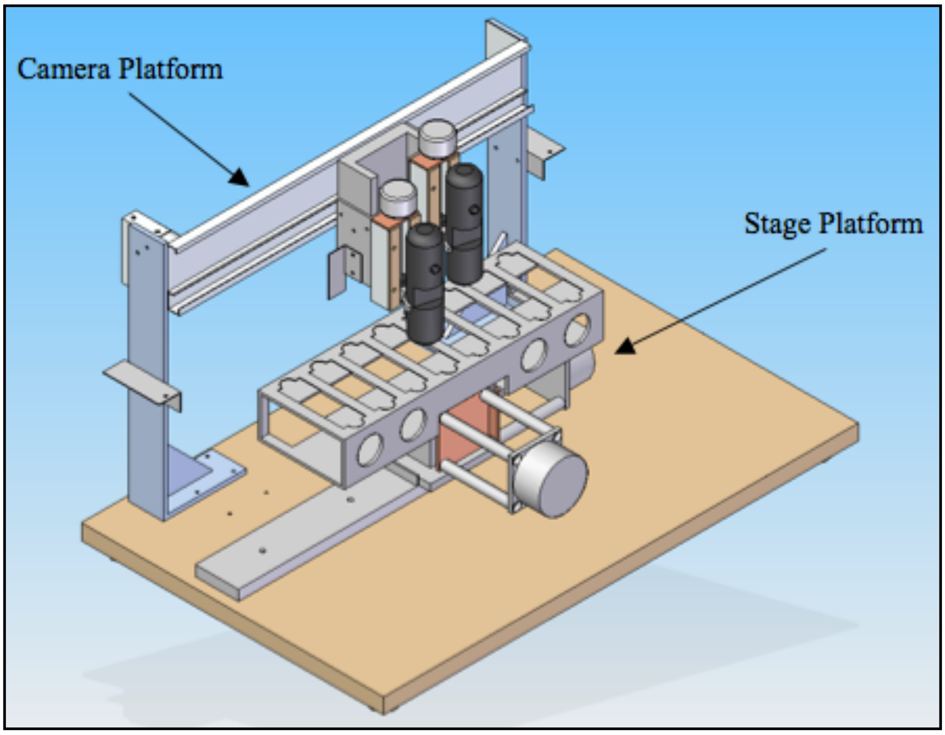


Figure 2: A CAD model of the microscope system created by Mr. Yilun Fan [1]

The system consisted of a stage, holding multiple slides in a row, that was capable of actuating horizontally (in both the X and Y directions) to manipulate the slide position. Mounted above the stage, on a rail, were two USB microscopes that were prefocused for magnifications of 20x and 200x. Slide changing was performed by moving the microscopes to the centre of different slides on the stage. Magnification changes were performed by moving the other microscope to the center of the slide. Both the camera rail and the slide platform actuators were recycled systems that were used in order to lower the cost of the system.

The electrical system was largely structured around the use of the ardiuno platform to reduce time in the prototyping stage of the project. Communication between the system and a client was facilitated through the use of an ethernet shield and the MQTT protocol: a protocol that allowed for text based communication between the client and the system.

Review

The project successfully proved that a low-cost computer controlled microscope could be implemented. The system demonstrated that the MQTT protocol could be used effectively to control the microscope over the internet. It also demonstrated an innovative use of micrometers and stepper motors to perform low-cost, high-precision slide manipulation.

The downfalls of this design were a lack of robustness and functionality. The camera rail for the system (a repurposed printer head carriage) lacked strength, which both greatly reduced the lifetime of the product and caused problems during development. In its current configuration a light source would have been difficult to add because it would need to move along the rail with the microscopes but remain centered on the slides when the magnifications were being switched. The system was also restricted to only two magnifications and the operator was unable to adjust the focus. These features could not be implemented because the camera rail could not take additional weight.

2.2.2 Control of a Remote Microscope Over the Internet: Merck Research Labs [5]

This project was designed to fulfill an increasing need for researchers to collaborate over the internet by allowing them to view and control a microscope remotely. The project was divided into three levels of control to meet different staff needs.

Phase I was to augment a Leitz Laborlux 12 Microscope with a camera so that remote clients could watch through the microscope. Because of bandwidth restrictions, the design used a timed capture system that transmitted photos every few seconds to a webpage that constantly refreshed. This refresh rate was maximized at once every four seconds for local clients and once every seven seconds for overseas clients.

Phase II implemented remote control of the microscope over the internet. The user had control over the slide platform position and magnification. Because of the significant image delay experienced by the user the system was designed to either move to specific coordinates or to increase/decrease the current position by 100um (at 400x magnification). The user also had access to an auto focus function.

Phase III added a slide loading mechanism capable of switching between 15 different slides (figure 3). The system consisted of a slide rack that was driven by a DC motor and pinion gear. Optical sensors worked as an interlock to ensure slides were centered correctly.

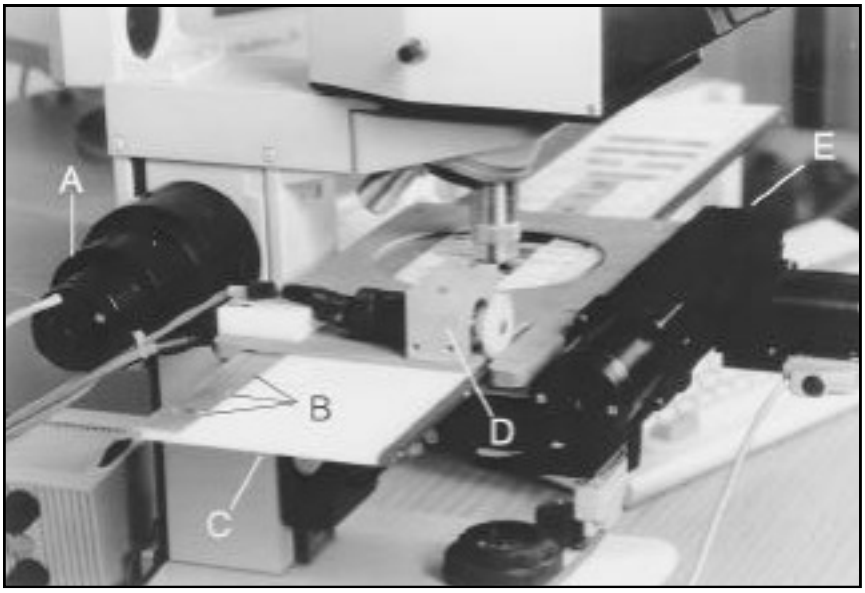


Figure 3: "Custom built slide loader. (A) Ludl autofocus controller motor, (B) optical sensors, (C) 15-slide microscope tray, (D) spring-loaded, geared motor unit and (E) Ludl x-axis/y-axis motorized stage." [5]

Review

Merck Research Laboratories successfully instrumented an existing microscope to be controlled over the internet. They managed to created a low-cost slide changing mechanism that could be augmented onto any system without other changes having to be made. Despite bandwidth limitations they also managed to create a system that would function satisfactorily in collaborative research when a researcher was working at the station.

The main drawback of this system was slow rate of transfer of images to remote observers. Because of the large delay this system would function very poorly when remote operators were attempting to locate objects on slides. In addition, the high cost (~$34000), while acceptable for developing research equipment, is prohibitively expensive for a school level system. However, the cost can mostly be attributed to the microscope itself and the high precision motors used to automate it.

2.2.3 Virtual Microscopy: M. Triola and W. Holloway [6]

This project took an alternate approach to teaching microscopy to students. Rather than giving students the opportunity to use a microscope, over 1000 slides were scanned and stored in a database as Google Maps formatted images. A basic GUI (figure 4) was created for students to access and explore the slides.

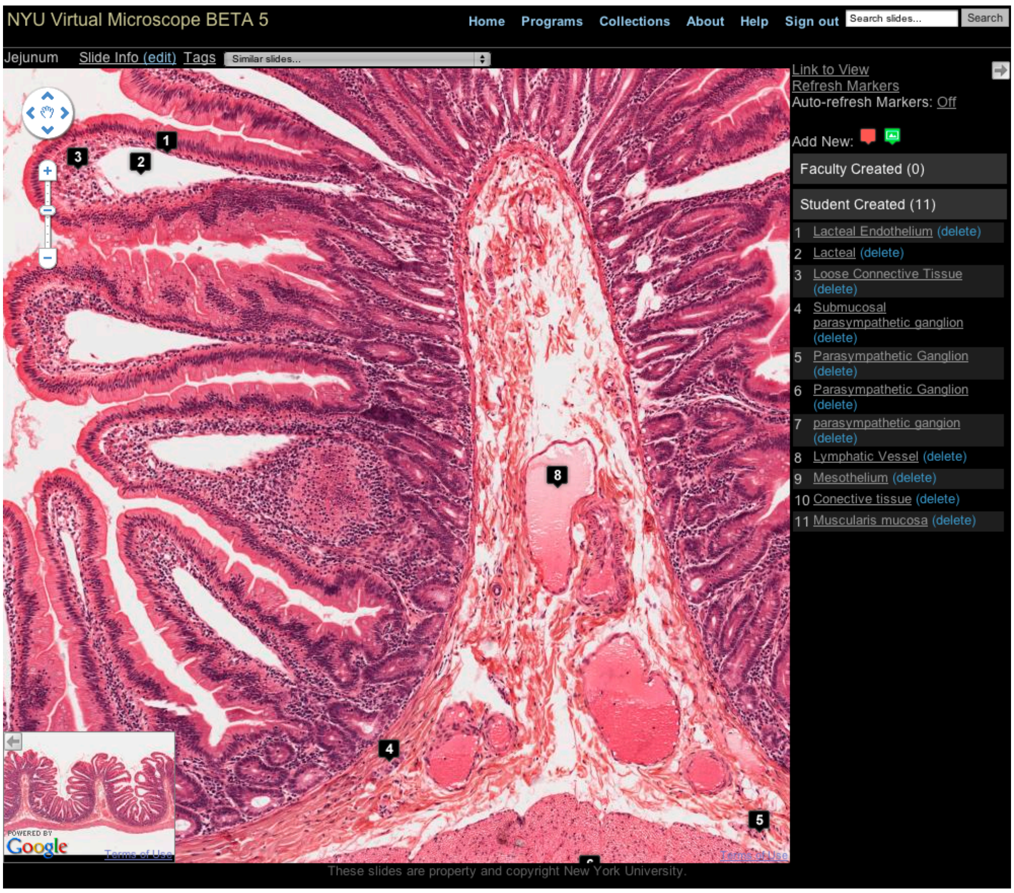


Figure 4: A virtual microscope GUI. [6]

Additional functionality included the ability for students and staff to annotate the slide with a number, name and short description. All students could see these tags and up or down vote them based on whether or not they were correctly labeled (and with sufficient down-votes tags would be removed). An exam mode was included as well, whereby students were given a set of slides that they were required to label appropriately in the time given.

Discussion

Virtual microscopy is a very powerful tool in teaching students identification techniques and better than physical microscopy in many ways. It gives students a chance to work at their own pace rather than being pressed to share a limited number of microscopes within designated class hours. It also gives students a chance to collaborate more effectively as they can all view identical slides and quickly move between tagged elements on the slides.

The system did have limitations. Students were limited to viewing slides in one focal plane: an obstacle that cannot be overcome without vastly increasing the database’s memory space. Students were also only able to view static images and not dynamic processes that can be viewed with a physical microscope. In addition students miss out learning how to use a physical microscope and these skills are often required in research projects and internships [6].

2.2.4 Positives and Negatives of the Systems

Table 1 shows a comparison of the systems reviewed in the previous sections. Table 1 was used in the design of the desired functionality (Section 1.3).

Table 1: A qualitative breakdown of the positives and negatives of the reviewed systems

System	Pros	Cons
2.2.1 (proof-of-concept system)	- low cost - easily interpreted communications - high precision slide movement	- not robust - insufficient functionality
2.2.2 (collaborative research system)	- modular slide changer - precision control can be done with a high ping	- high cost - poor communication speed
2.2.3 (virtual system)	- high level of repeatability - easy remote collaboration	- no physical microscope practice - no dynamic process viewing - only one focal plane

3. Project Plan

The plan for this project was developed by breaking up the mechanical, electrical, software and literary aspects of it into smaller, logical tasks. Because of the complexity of this project it was difficult to predict an accurate division of the workload, so instead, the focus was to determine what tasks were dependent on each-other. Tasks and their dependancies can be seen in table 2.

Table 2: A breakdown of the project tasks and how their dependancies on each other

#	Category	Task	Dependencies
1	Mechanical	Design of the moving slide platform	-
2		Design of the magnification adjusting system	-
3		Design of the focusing system	-
4		Design of the mechanical framework	1, 2, 3
5		Fabrication of parts	4
6		Assembly of mechanical system	5
7	Electrical	Selection of the controlling chip	9
8		Selection of the motors	1, 2, 3
9		Selection of the motor controller ICs	8
10		Design of the motor controlling schematic	9
11		Fabrication of the motor controller circuit	10
12		Selection of the computer interface chip	7
13		Assembly of electromechanical system	6, 7, 11, 12
14	Software	Implement/source motor controlling software	7
15		Select communication protocol	-
16		Implement server/client communication scheme	7, 15
17		Design web-based control interface	4, 15, 16
18	Literary	Review/deployment of product	13, 14, 16, 17
19		Thesis writeup	18

A timeline was estimated by grouping the tasks listed in table 1 into logical milestones. An optimistic time was then allocated to each milestone based on the goal of product completion by the end of semester 1. The timeline can be found in appendix A.

The black, low-risk, resource independent tasks make up the majority of the workload of this project. These are tasks that only require computers or basic hand tools that are readily available.

Tasks coloured red signify that they are highly dependent on services that take a very variable amount of time. These include:

- Machining of mechanical parts
- Sourcing of mechanical and electrical parts
- Delivery of ordered parts
- PCB manufacturing

The deployment task is coloured blue because it requires a schools participation. Whether or not this is available at the required time will be highly variable but it is not classified as a high-risk task because it is not an required task for project completion.

4. OHS Risk Assessment

Work on this project is to be undertaken in 78-420 which is classified as a **Low Risk Laboratory**. As such it is covered under the general OHS laboratory rules.

5. Bibliography

[1] Yilun, F 2011, ‘Computer Controlled Microscope’, BE thesis, University of Queensland, Brisbane.

[2] Raja, S 2010, ‘Virtual microscopy as a teaching tool adjuvant to traditional microscopy’, *Medical Education*, vol. 44, no. 11, pp. 1126.

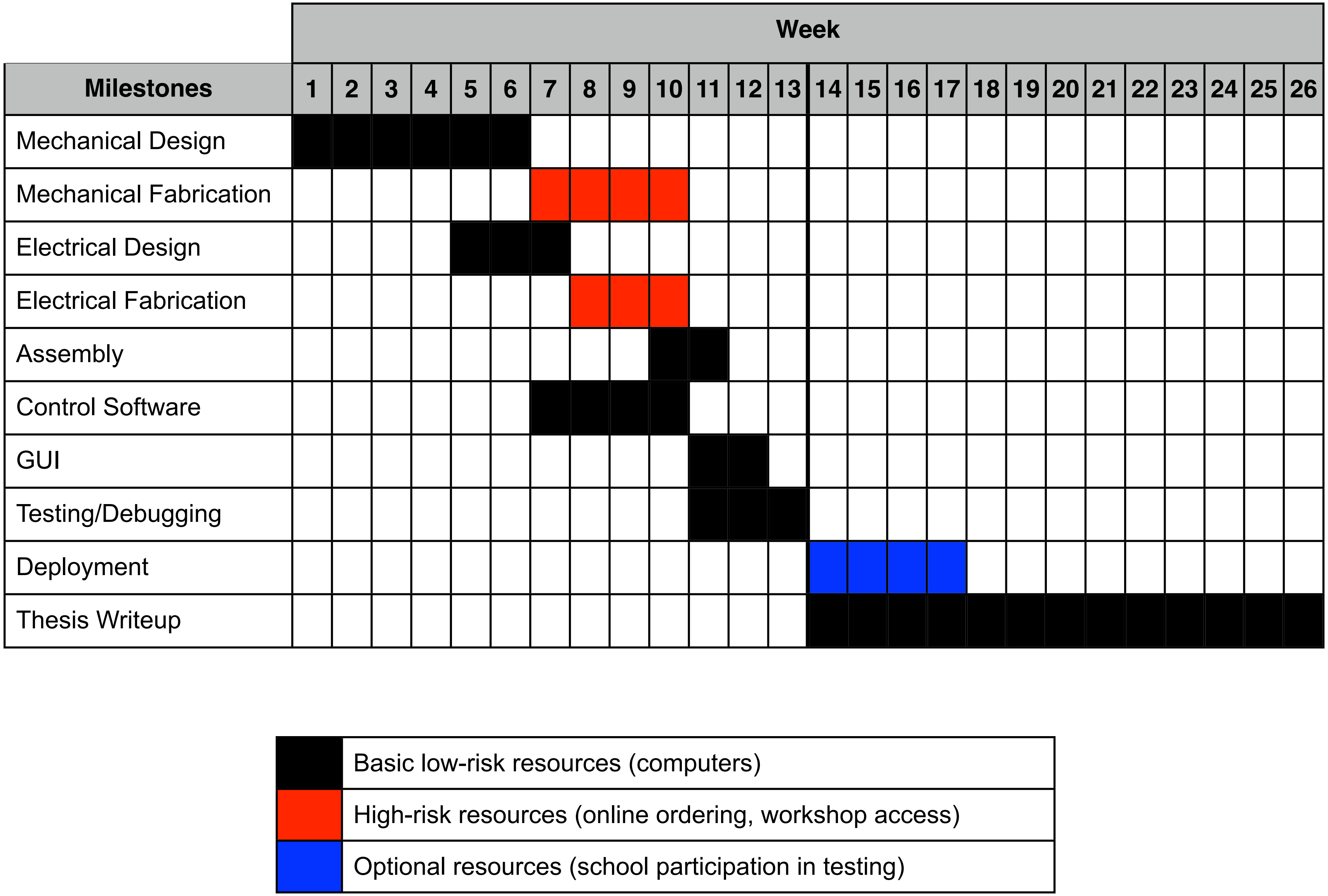
[3] Kumar, S & Dunn, BE 2009, *Telepathology,* Springer, Berlin.

[4] Quercioli, F 2011, ‘Fundamentals of Optical Microscopy’, *Optical Fluorescence Microscopy,* Springer, Berlin.

[5] R. Maturo, G.Kath, R. Zeigler and P. Meechan, 1997, ‘Control of a Remote Microscope Over the Internet’, BioTechniques, vol. 22, No. 6, p1154.

[6] Triola, MM & Holloway, WJ 2011, ‘Enhanced virtual microscopy for collaborative education’, *BMC Medical Education,* vol. 11, no. 1, pp. 4.

6. Appendix A


Week
Milestones
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26
Mechanical Design
Mechanical Fabrication
Electrical Design
Electrical Fabrication
Assembly
Control Software
GUI
Testing/Debugging
Deployment
Thesis Writeup
Basic low-risk resources (computers)
High-risk resources (online ordering, workshop access)
Optional resources (school participation in testing)