My interest in emergency medicine technology developed as a result of my training to become an Emergency Medical Technician (EMT). It was this interest that led me to the University of Washington's Bioengineering Department and to the study of microfluidics[1]. While exposing me to the magic of emergency medical care, my EMT training also revealed to me the shortcomings of the industry. It is my belief the many of these shortcomings can be eliminated with the development of novel biomedical devices. One of my greatest, long-term professional goals is to produce microfluidic devices that put the abilities of the hospital into the hands of the paramedics. The yield of my current work should find applications in this regard.

Microfluidic devices have shown great potential for providing point-of-care (POC) solutions for diagnostics, food and environmental safety, and forensics[1,2]. At the same time, their impact on these fields has been limited by their general requirement for the supporting behaviors of bulky and expensive laboratory equipment such as computers and air pumps. The elimination of a device's dependency on this peripheral equipment is perhaps the greatest challenge in developing marketable POC solutions for the home or for the developing world. In an effort to provide a platform for the construction of microfluidic technologies with reduced laboratory dependencies, the proposed project aims to produce an on-card fluid delivery system suitable for use away from the lab. This system will be capable of directing a multi-step assay and will require only an electrical input of variable frequency to operate. Because this input can be provided by a cellular phone, or some other similar piece of personal equipment, the system will allow for the development of devices that are practical for use in the home or in the field.

The system will employ fluidic oscillators, analogous to AC electrical circuits, with piezoelectric actuators to give frequency-specific flow control[3,4]. Constructed from mostly glass and plastic materials, the envisioned system offers the benefits of small size, low-cost manufacturing, portability, and durability. These are benefits that simply cannot be provided by the more typical laboratory fluid control systems which employ large and expensive pumps to drive fluid and open

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[1] Microfluidics is a field that deals with the engineering of fluid systems with dimensions on the micrometer scale

or close on-card valves[5-8]. In contrast to paper-based microfluidic products, the system should offer high operating speeds and be tolerant of a wide range of chemical reagents. A successful project effort will yield a product with the potential to elicit the commercialization of any number of microfluidic technologies currently tethered to the laboratory environment.

The project has been developed as a senior capstone project in accordance with the guidelines set forth by the UW Bioengineering Department's Undergraduate Affairs Committee. As a result, my work on the project will be highly individual. I will be responsible for the design, construction, and testing of all prototypes. Dr. Paul Yager of UW Bioengineering will provide access to his facilities and to the materials and equipment necessary for my work. Dr. Barry Lutz, also of UW Bioengineering, will serve as a constant mentor, offering aid in the problem solving process. To date, Dr. Lutz's commitment to the success of my project as a learning tool has done much to increase my understanding of the research process and its role in the biomedical industry. Through my work on this multidisciplinary project I will be pushed to learn about aspects of mechanical, electrical, and chemical engineering as well as public health, immunochemistry, and business. It will be the single greatest source of learning in my undergraduate career.

In order to achieve the overall project goal, a number of steps will need to be taken. These steps are presented here as the specific aims of the project.

The first specific aim is to design and construct a single microfluidic oscillator[2] capable of converting oscillatory fluid flow to unidirectional fluid flow at a specific frequency range. Such behavior will allow for the input signal to select for flow from the oscillator by providing an AC electrical input of the appropriate frequency. The fluidic oscillator will employ a piezoelectric actuator for oscillatory fluid displacement and otherwise will consist of passive fluid channel features acting as the fluidic equivalents of the electrical resistor, inductor, or capacitor. In essence, the oscillator is an RLC band-pass circuit in connection with a fluidic diode (or one-way valve) that

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[2] An oscillator is the combination of the piezoelectric actuator and the glass or plastic features that allow for conversion of oscillatory flow to unidirectional flow.

will create unidirectional flow from oscillatory flow at input frequencies near the resonant frequency[3] of the circuit. A fluid reservoir will be connected to the circuit to allow for maintained unidirectional flow. Performance targets for specific aim one include a maximum net flow rate greater than 10 microliters per minute and a flow rate of less than 5 percent of the maximum when the input frequency is more than 50 hertz from the oscillator resonant frequency.

The second specific aim is to design and construct a device for a multistep assay. This device will contain three fluidic oscillators, each with distinct resonant frequencies. They will be wired to share a single electrical input and their output pathways will be made to converge into a common duct. This will allow for a user to control the mixing of three different reagents by varying the frequency of the input signal to select for flow from the individual oscillators. For simplicity, the success of aim two will be demonstrated with colored dyes. The system will be designed for the crosstalk at each resonant frequency to be less than 1 percent. Crosstalk is defined as the total net flow from oscillators other than the one being selected for by the input signal.

Finally, the third specific aim will be to modify the aim two device so that it can be used to carry out the catalase reaction. This will demonstrate how the device might be used for the detection of disease. For this, the oscillator system will need to control the flow of three fluids: 1) a fluid containing biotinylated catalase[4], 2) a wash fluid, and 3) hydrogen peroxide. A port, or basin, will be built into the common output duct and the walls of this port will be coated with immobilized streptavidin[5]. When the biotinylated catalase is passed through the port it will bind to the streptavidin and will be retained to react with hydrogen peroxide for the production of bubbles. This bubble producing mechanism can be directly tied to the detection of proteins and thus used for the diagnosis of disease. Because the scope of the present study must be limited, this coupling is not a

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[3] The resonant frequency of a system is the frequency at which the system oscillations have the greatest magnitude.

[4] Catalase conjugated to biotin. Biotin is a vitamin that binds strongly to streptavidin.

[5] Streptavidin is a tetrameric protein used commonly in molecual biology because of its affinity for biotin.

goal of the project. The success of the effort to achieve aim three will be evaluated based on visual detection of bubbles produced in the port.

If all three specific aims are accomplished, the result will be a demonstrated route to market for many laboratory-restricted microfluidic technologies. These technologies would find applications in food safety, environmental analysis, forensics, emergency medical care, home healthcare, biothreat detection, and diagnostics.

After graduation, I plan to travel. This travel will be designed to allow for me to gain first-hand experience with the healthcare industries of the developing world. Such experience will help me to identify the specific needs of these industries and should shed some light on how I might address those needs through microfluidics. Perhaps, I will discover immediate applications for the products of my current work.

Upon returning from my travels, I will apply to medical school. My goal to become a medical doctor is also directly related to my current project. Specifically, I aim to be a cardiologist. As a cardiologist, I would be interested in the development of biomedical technologies for health care in the home. Such technologies have the potential to greatly reduce healthcare costs and in this way provide relief to the many Americans that struggle to afford care. There are a number of social and ethical issues involved with the production of such technologies. An example is the ethical dilemma associated with providing an inexpensive diagnosis for a disease that requires expensive treatments. As a doctor, my work to develop new biomedical technologies would be guided by a moral compass.

I am extremely excited about my project and I trust that it is clear as to why. The project will do a lot to prepare me for achieving my educational and professional goals. In addition, it has the potential to yield products of great benefit to consumers in healthcare industries worldwide. I sincerely hope that you can choose to support me in my efforts. Thank you.

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