Anophelseize

A Target Malaria Collaboration

Bioengineers Without Borders

Holloman Health Innovation Challenge 2018

Business Plan

University of Washington

Concept

In 2004, the Bill & Melinda Gates Foundation launched the Grand Challenges in Global Health as part of a research initiative to tackle health problems throughout the world[1]. One of the challenges that has grown tremendously since the launch is the technological development for malaria control. As part of Bioengineering Without Borders at the University of Washington in collaboration with the Target Malaria Research Consortium and the Uganda Virus Research Institute (UVRI), we have designed Anophel*seize*. Anophel*seize* is an efficient, low-cost capturing device for male mosquitoes of the species *Anopheles gambiae* to be used for field research.

Problem

The current state of malaria research is limited by mosquito collection in the field. Researchers must go out at night with carbon dioxide or light traps and manually capture the insects for study. Female mosquitoes will follow these signatures as they would to find prey, but male mosquitos are not attracted to carbon dioxide, so another method must be used to capture them. Existing methods for male mosquito capture are more limited and less reliable in comparison to traps for females. Malaria is transmitted by female *Anopheles gambiae* mosquitoes, thus more research has been done involving the capture and study of females. Although current traps allow for analysis of the disease vector, male mosquitoes still have a role in the pathogenesis of malaria through breeding. The capability to capture male mosquitoes would allow for population and breeding pattern studies of the *Anopheles*. Our contacts at the UVRI are also interested in capturing male mosquitoes for future research in gene editing of this species of mosquitoes in hopes of eradicating the spread of malaria.

Solution

Our proposed solution for capturing male *Anopheles gambiae* mosquitoes for research is a device that utilizes an acoustic mechanism to attract and capture the mosquitoes of interest. Recent research has shown that male mosquitoes can be efficiently attracted to speakers that emit an audible frequency that mimics the wingbeat of females[2]. A frequency of 400 to 500 Hz, that mimics the frequency produced by female mosquitoes' beating wings, is emitted from the device to potentially attract males, as they normally follow this acoustic signal in order to mate. To emit this frequency, a small battery-powered speaker is attached to the inside top surface of

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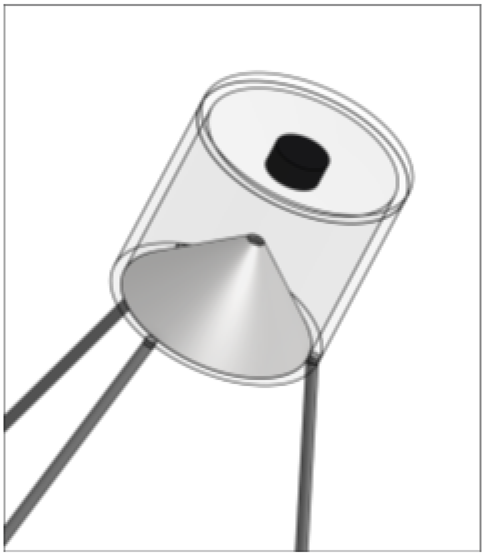
[1] Gates Foundation Grand Challenges Breakthrough Science. (2014, October 7). Retrieved February 02, 2018, from https://www.gatesfoundation.org/Media-Center/Press-Releases/2014/10/Gates-Foundation-Grand-Challenges-Breakthrough-Science

[2] Johnson, B. J., & Ritchie, S. A. (2015). The Siren's Song: Exploitation of Female Flight Tones to Passively Capture Male Aedes aegypti(Diptera: Culicidae). Journal of Medical Entomology, 53(1), 245-248. https://doi.org/10.1093/jme/tjv165

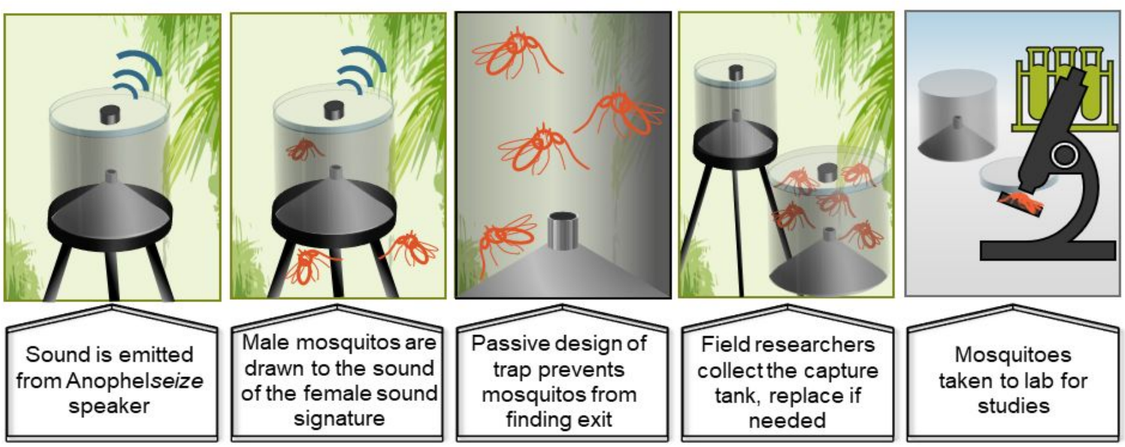
a non-biodegradable, cylindrical container approximately 20 centimeters in diameter.



Schematic of trapping mechanism and containment unit for Anophelseize. The speaker is represented by the solid black cylinder.

The bottom of the cylinder has an inverted funnel shape with an opening of approximately 2 centimeters that allows for the passive capture of the mosquitoes. The mosquitoes will be able to follow the emitted frequency and easily enter the device, but due to both the mosquitoes' tendency to remain on the edges of enclosures and the small size of the opening, they will have difficulty exiting. Having the opening of the inverted funnel on the underside of the trap will also help to protect from weather and rainfall.

The device is mounted on a tripod stand made of PVC piping approximately 100 centimeters in height to limit possible weather, flooding, or wildlife interference. The mount of the tripod is a ring that fits around the bottom of the cylindrical container to prevent blocking the entrance of the inverted funnel. The container is detachable from the ring mount so that when it is full of mosquitoes it may be replaced with an empty container. This will not only allow for continuous capture of mosquitoes but prevent the need to frequently transport the tripod stand, as it can be reused. To ensure ease of transport when initially placing the tripod in the field, the legs of the tripod are retractable and collapsable.



Market & Existing Products

Traps that emit carbon dioxide or animal-like odors are very effective for catching female mosquitoes and are used widely in the field[3], but male mosquitoes are caught in minimal quantities simply because they feed on plant nectar and are not searching for a blood meal.

[3] Ndiath, M. O., Mazenot, C., Gaye, A., Konate, L., Bouganali, C., Faye, O., Sokhna, C., Trape, J.-F. (2011). Methods to collect *Anopheles* mosquitoes and evaluate malaria transmission: A comparative study in two villages in Senegal. *Malaria Journal*, *10*, 270. http://doi.org/10.1186/1475-2875-10-270

There are no existing products capable of selectively attracting and trapping male mosquitoes. Most research done on wild mosquito populations has captured male mosquitoes through active, work-intensive methods such as sweep-netting mating swarms and sorting caught mosquitoes individually by sex, or through isolating the small percentage of males who are caught in conventional mosquito traps. Our trap provides a means of passively yet selectively collecting male mosquitoes over a week, which allows researchers to sample mosquito populations from many different locations without extensive hands-on time. We envision three potential markets for our male mosquito trap. All depend on environmental monitoring of *Anopheles* mosquito populations, but for three different purposes, all with the ultimate goal of reducing the burden of malaria.

The first purpose is monitoring of natural populations in malaria-endemic areas, to enable better predictions of malaria epidemiology and to provide preliminary data for the planning of mosquito eradication programs. This is the current goal of the Uganda Virus Research Institute, who estimate their need to be 20 traps, a market size of roughly $5,000 if we sell at cost. The second market for male mosquito traps is to monitor the efficacy of trials of the Sterile Insect Technique (SIT), in which sterilized male mosquitoes are released to reduce wild mosquito populations. This technique has been used in various programs to eradicate insect pests, and is now being used in pilot programs throughout Africa to eradicate *Anopheles* mosquitoes[4]. It is important to sample male mosquitoes to determine the number and distribution of sterilized males to release, and later to evaluate the efficacy of such trials. We estimate the market for male mosquito traps to monitor SIT trials around the world to be roughly 100 traps, which we could sell at cost for $25,000 total. The final market for capture of male *Anopheles* mosquitoes is to monitor the effectiveness of a gene drive. Gene drives are an experimental technique in which a gene is introduced to *Anopheles* mosquitoes that could perform a function such as skewing the sex ratio of offspring, and would propagate through multiple generations until a population of wild mosquitoes is dramatically reduced and malaria is eradicated from the region. This technique has not been tested in the wild before, but is the goal of Target Malaria, a daughter project of the Bill & Melinda Gates Foundation[5], and may become another market for male mosquito traps in the near future. The size of this market depends on the success of initial trials, but may be comparable to the SIT market ($25,000).

Projected Cost and Customers

Our research team is currently collaborating with the UVRI to solidify an applicable design to fit the needs of the researchers equipped to utilize our device. Since our device will be used for a very unique market, our customers will be limited to research institutions requiring male mosquitoes for research databases, observation, and/or direct manipulation. Anophel*seize* will be able to fulfill the unmet needs of customers within a niche market who will be using our product for malaria research and other tropical diseases spread through contact with

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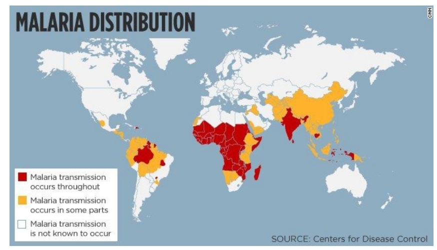
[4] International Atomic Energy Agency, Insect Pest Control. (2015). Male mosquito trapping methods. *IAEA Technical Report.* Retrieved from <http://www-naweb.iaea.org/nafa/ipc/public/Technical-Meeting-Report-Male-mosquito-trapping-methods.pdf>.
[5] Regalado A. (2016, September 6). Bill Gates Doubles His Bet on Wiping Out Mosquitoes with Gene Editing. *MIT Technology Review.*

mosquitoes. Currently, our collaborators at UVRI plan to purchase 20 units of Anophelseize, which allows them to collect data for two villages at a time. There is also potential to produce many more units, as malaria affects 106 countries and territories worldwide[6].

Globally, the CDC estimates that direct costs due to malaria total at approximately 12 billion USD per year, and indirect costs such as lost economic growth and preventative measure add much more to that per annum total. In Uganda alone, the economic cost of malaria has been estimated to be at minimum 204 million USD per year[7]. To combat malaria, as part of the Uganda Malaria Reduction Strategic Plan, Uganda has allocated 0.73 million USD towards strengthening capacity in entomology, epidemiological surveillance, insecticide resistance monitoring, vector behaviour and bionomics from 2018 to 2020[8].



In order to combat malaria, it is first necessary to better understand the behaviors and ecological impacts of mosquito populations. Current malaria research is mostly focused on female mosquito populations and more information is needed on male mosquitos. One of the goals of Target Malaria is to eventually run sterile insect trials on male mosquitoes. Our device would allow researchers to look at the ecological impact of sterilizing male mosquitoes and evaluate whether male mosquito sterilization is a viable way to eradicate the spread of malaria. Our device will enable researchers to more easily capture and study the population size and movements of male Anopheles. There is a growing need for easy-to-use, cost effective mosquito traps that can be used in low resource settings. Considering our consumers are a relatively small and specific set of researchers, our device will be cheap to manufacture, easy to implement, and effective in its ability to trap mosquitoes. This is also a trap designed with global health constraints in mind which means the cost must be as low as possible, while still ensuring the integrity of the trap. It is designed to be easy to transport, and it will be built with simple parts to ensure that maintenance costs are low. Having an open source business plan will help reduce cost, which will allow the researchers we are trying to help make the biggest impact on the progression of mosquito research at a very low cost.

The initial estimated cost for each device is approximately $250 for materials, not including labor. Based on preliminary customer plans, 10 devices will be deployed in each village/location, resulting in an approximate cost of $2500 for each location. Specific quantities can be customized by the customer and costs are likely to decrease as the number of commissioned devices increases. Shipping costs from major US cities to Uganda, for example, come to $3.50 per pound, and similar rates apply for South America and other malaria-affected areas.

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6 Malaria. (2017, December 20). Retrieved February 05, 2018, from https://www.cdc.gov/malaria/malaria_worldwide/impact.html

7 National Malaria Control Program. (2018). Retrieved February 05, 2018, from http://health.go.ug/programs/national-malaria-control-program

8 THE UGANDA MALARIA REDUCTION STRATEGIC PLAN 2014-2020. (2014, May). Retrieved February 05, 2018, from health.go.ug/download/file/fid/526

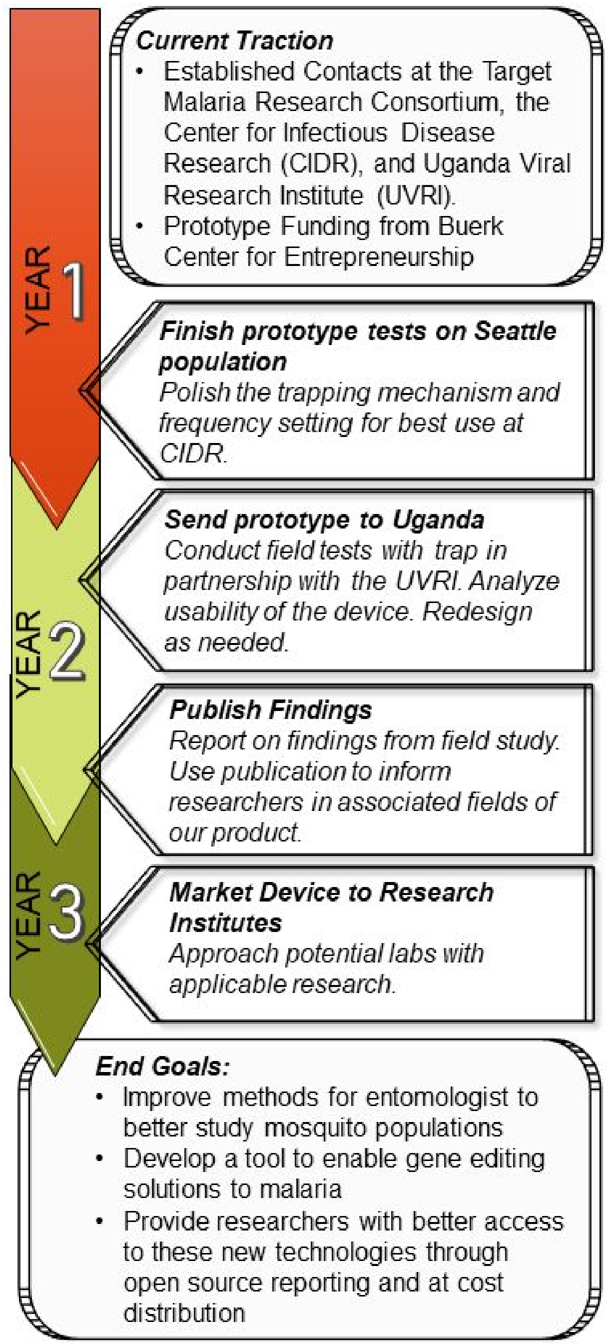
Long Term Strategy

We plan to make Anophel*seize* available to field researchers within 3 years. Our current traction in development of this device has allowed us to design our initial design and fabricate our prototype through funding by the Buerk Center for Entrepreneurship.We have also established relationships with CIDR and UVRI, allowing us access to test mosquito populations locally and abroad.

These initial proof-of-concept tests on the *Anopheles stephensi* population in Seattle will be completed in year one. Prototype tests in Uganda on Anopheles gambiae will be conducted in year 2 with UVRI. We plan to publish findings at the conclusion of year 2.

Due to our role in research, we find it is valuable to keep our design open source. This will provide greater access to this technology to researchers globally. As a company we will sell the Anophel*seize* at cost of components and labor.

We believe this business model will develop better relationships with research institutions with applicable scientific interest, who would otherwise not have the technical expertise to build a similar trap. We also hope this model will open opportunities for funding sources by the Center for Disease Control or other government-funded agencies.



Project Team

Jamie Hernandez is a second-year Ph.D. student researching low cost devices with global impact in the Woodrow Lab at the University of Washington. She graduated with a B.S. in Biomedical Engineering and a minor in mathematics from the University of Arizona.

Ian Hull is a first-year Ph.D. student rotating in the Lutz and Woodrow Labs at the University of Washington. He holds a B.S. in Bioengineering from Stanford University. His current research is focused on developing an instrument-free device for HIV viral load monitoring.

Colleen O'Connor is a first-year Ph.D. student interested in using bioprinted tissue to study liver regeneration and disease in the Stevens Lab at the University of Washington. She graduated from The University of Texas at Austin with a B.S. in Biomedical Engineering.

Anna Klug is a third-year undergraduate student in the Department of Bioengineering at the University of Washington. She is currently researching stem cell therapies for cardiovascular regeneration in the Murry Lab at the University of Washington.

Eric Yang is a second-year undergraduate student researching biomaterials for stem cell differentiation in the Bioengineering department at the University of Washington.

Kira Evitts is a third-year undergraduate student in the Department of Bioengineering at the University of Washington. She is currently doing research in modelling the pathology of Alzheimer's Disease using neural stem cells in the Young Lab.

Mitchell Ekdahl is a second-year undergraduate student in the department of Bioengineering at the University of Washington. He is currently interested in the development and implementation of global health solutions in low- and middle-income countries.

Kate Hawkins is a second-year undergraduate student at the University of Washington. She is a prospective Microbiology major interested in the epidemiology of infectious diseases.

Troy Friedman is a second-year undergraduate student at the University of Washington. He is a prospective Bioengineering major.

Heather Klug is a third-year undergraduate student in the Department of Biochemistry at the University of Washington. She is currently researching drug-inducible gene activation in cardiomyocytes differentiated from transfected stem cells in the Murry lab.

Project Advisors

Dr. Ray Monnat is a professor of pathology & Genome Sciences at the University of Washington. He has advised our team with the project need and long term application of this device to gene editing.

Dr. Jonathan Kayondo is a Senior Research Officer at UVRI, who has provided our team with insight into how this field research is conducted and the need for improved tools for field entomologists.