MI-Dengue: A novel tool for dengue vector monitoring in Brazil

Recent estimates predict over 300 million cases of dengue fever occur every year, transmitted by the *Aedes sp.* mosquito vector. The disease causes high fevers, headaches, muscle pain, and a characteristic rash. In severe cases, the disease can progress to dengue hemorrhagic fever, resulting in bleeding and blood plasma leakage, and even death. Brazil is especially hard hit by this disease with over 1 million cases reported in 2010. Cases in 2013 are also set to break the record with 714,000 cases already notified as of April 2013, reported by the Brazilian Ministério da Saúde.

Without a vaccine, it is critical to control the presence of the mosquito vector, *Aedes aegypti* and *Aedes albopictus* female mosquitos (Figure 1). The Brazilian government spends more than US$1 billion annually in an effort to reduce the incidence of dengue. However, the methods used have so far not proven effective in halting the spread of the disease. One factor that might contribute to this is the time-delay between vector monitoring and control implementation. The immature larvae form of the vector is monitored, but the data takes weeks to analyze and the process can only be completed at best, four times per year. By then, the mosquitos may have gone through several life cycles and the areas with critical mosquito populations may have relocated. To solve this problem, the MI-Dengue monitoring system was developed by Ecovec. By monitoring the adult vector weekly and identifying the presence of the virus in the mosquito, Ecovec can predict the risk of an outbreak four to eight weeks in advance and spatially and temporarily optimize vector control actions.

History of Ecovec:

After 20 years as an entomological researcher, Professor Alvaro Eiras (PhD) decided to put his knowledge to the test and create a product to help defend the population against mosquito transmitted diseases. He wondered if it was possible for each Brazilian family to have a trap to capture the

Figure 1: Female Aedes aegypti mosquito, the principal vector of dengue.

dengue fever mosquito vector in their home. Thus, he decided to talk with Paulo Renato, at that time, the leader of the start-up incubator at the Federal University of Minas Gerais (UFMG). Paulo Renato saw the value in Prof. Alvaro's research and decided to join him on his journey. With the help of *Instituto Inovaçao*, a start-up accelerator who developed "Innovation Diligence", a specific methodology for technology assessment, Prof. Alvaro came to realize that the "sticky trap" he was developing had a better fit: to enable public authorities to monitor and measure the risk of a dengue outbreak. The market potential of this new solution appeared to be large, so

Figure 2: CEO Gustavo Mamão and Founder Dr. Alvaro Eiras receive the Edison Award for improving "Quality of Life" in 2013.

Instituto Inovaçao decided to offer support by investing in the development of a complete dengue monitoring system. The Brazilian government bought into the idea as well, and over time invested more than US$2 million in grants to fund the innovation. After three years of hard work, the system was complete and named MI Dengue for Intelligent Monitoring of Dengue. Ecovec, the start-up founded, then introduced its service to the market and secured its first commercial client in 2005.

With increased implementation of MI-Dengue in the following years, it became clear to the Ecovec team that an additional tool was needed to enhance the MI-Dengue system: knowledge of viral infestation status of mosquitos. Ecovec gathered a group of innovators to research, develop, and commercialize a way to analyze mosquitos for dengue virus presence. The team quickly became experts in dengue virus detection, and used biomolecular viral analysis concepts from academia to commercialize a viable service within three years. The MI Virus service developed uses the latest technology in viral analysis combined with an innovative logistics system to preserve the mosquitos during transport from trap to laboratory.

MI-Dengue has since been implemented in diverse locations throughout Brazil. An interesting example is a project with the state of Minas Gerais in 2009 to provide MI-Dengue in 27 cities with high risks for dengue epidemics. The project generated two years' worth of data that was then used to study the cost-benefit of MI-Dengue in reducing the dengue burden on the population. Positive results encouraged the further spread of the system. Among Ecovec's current clients are the urban centers of Porto Alegre, a large city in the southern region of the country; Santos, the largest port in South America; and Vitória, a coastal city and major tourist destination. In recognition of its efforts against dengue in Brazil, MI-Dengue received the Edison Award for improving "Quality of Life" in 2013
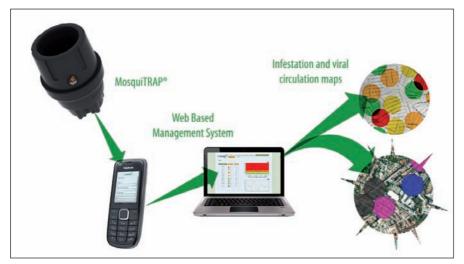
Figure 3: The MI-Dengue system is composed of MosquiTraps to capture dengue vectors; a web-based information management system to automatically process data; and maps, graphs, and charts that demonstrate vector density and viral circulation throughout the city.

(Figure 2). MI-Dengue has also been well received internationally in countries that are threatened by dengue. Australia, Singapore, Hawaii, Portugal, and Colombia have tested the system in key cities to evaluate the viability of MI-Dengue in diverse international climates.

MI-Dengue

The MI-Dengue system provides real-time information about the presence, population dynamics, and viral load of *Aedes aegypti* and *Aedes albopictus* dengue fever vector population in urban areas for all 52 epidemiological weeks per year. The system is implemented citywide and the vector population information is used by government vector control departments to optimize vector control activities.

MI-Dengue works through the following steps (also shown in Figure 3):

Trap Deployment: First specially designed traps for the dengue vector called MosquiTraps are placed in a grid every 200m across the urban area of the city to be monitored. The traps are placed using GPS and their exact location is recorded using special mapping software. A field worker placing a trap is seen in Figure 4.

Vector Capture: Next, the MosquiTraps lure the adult vector through its imitation breeding-site design. Blood-fed female *Aedes aegypti* and *Aedes albopictus* mos-

quitos enter the trap in an attempt to lay eggs but instead become trapped on the adhesive surface of the sticky card. The mosquitos remain trapped until government field workers make their weekly visit to collect the vectors. To increase vector capture rates, a patented synthetic semiochemical is used in combination. The semiochemical was developed and patented by the Laboratory of Chemical Vector Ecology at UFMG and has had success in attracting primarily gravid female vectors of dengue. The MosquiTrap is shown in Figure 5.

Data Collection: Once captured, weekly vector counts are made by field workers and sent electronically via mobile devices to a central database. The mobile devices used for data collection are low-cost for field use and use proprietary software for real-time data entry and transfer. The field workers record the species of each mosquito captured as well the gender. Because *Aedes aegypti* females (the principal vector of dengue) are easy to distinguish from other mosquito species in Brazil, identification is made by naked eye, or using a magnifying glass to aid in identification. This step saves time compared to species identification in a laboratory setting and allows for real-time population data.

Data Processing: Once the data arrives at the central database, the information is automatically processed and weekly entomological indices are generated to present a predicted risk of dengue occurrence based on vector infestation. The entomological index called IMFA (Average Capture of Female *Aedes aegypti* Vectors) is calculated by taking the average number of captured female *Aedes aegypti* per trap inspected in a specific week. The risk prediction is classified by green or satisfactory (IMFA bellow 0.15), yellow or moderate (IMFA between 0.15 and 0.30), orange or alert (IMFA between 0.30 and

Figure 4: A field worker uses a GPS device to place a MosquiTrap and send its location to the central database.

0.60), and red or critical (IMFA 0.60 or higher) indicators. Risk indication is a result of historical studies considering the correlation between infestation index and dengue case occurrence probability. Infestation maps are also generated, highlighting areas of high vector population density to give control managers focus areas for chemical and mechanical control (Figure 6).

MI Virus (Viral Analysis): Finally the captured mosquitos are collected from the MosquiTraps and sent to a central laboratory where they undergo biomolecular testing for detection of dengue viral RNA fragments and serotyping for virus types DENV 1-4. Serotype is important to know because the entry of new serotype in a region can cause an epidemic if the population has never been exposed before. A specialized protocol developed by Ecovec using quantitative real-time reverse transcriptase polymerase chain reaction (qRT-PCR) is used to analyze the mosquitos. Pools are created to economize resources and provide the information as quickly as possible. Every positive pool result for dengue virus RNA fragments induces a new cycle of biomolecular analyses for each tube containing mosquitoes collected from one specific MosquiTRAP. Once the results of the
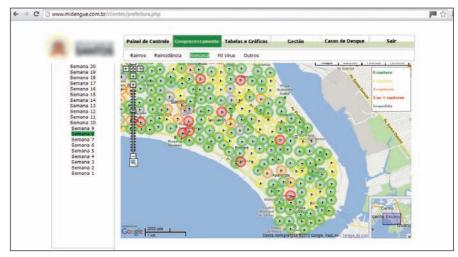

Figure 6: The mosquito density and viral circulation information is automatically presented on interactive maps. Green, yellow, orange, and red circles represent captures of zero, one, two, and three or more captures each.

Figure 5: The MosquiTrap is designed to capture the adult female Aedes aegypti vector of dengue. It attracts the mosquitos when they seek a suitable container for oviposition.

tests are known, the information is automatically integrated with the web based platform for the city vector control managers. Hence, local health manager are able to identify the exact location (block and street address) of dengue virus circulation with enough time to act for better vector control results.

Implementation Scenarios

Since the first client city of Congonhas, Minas Gerais, MI-Dengue has been implemented in 60 cities and covered a population of approximately 10 million people. The city of Vitória in the state of Espirito Santo has used MI-Dengue for 6 years since January 2007 and shows an interesting application scenario in an environment where dengue epidemics are a reoccurring problem. In Vitória, 1,410 traps are installed covering an urban area of 88 km^2 and a population of almost 400,000. The government control department relies on the information provided by MI-Dengue to prioritize chemical control areas and manage the vector population. Vitória is also interesting because the history of data shows a correlation with an increase in the MI-Dengue vector index IMFA and the occurrence of dengue epidemics in the city. Around four to eight weeks before an epidemic begins, it is possible to see an increase in the IMFA, meaning the vector population is growing.

MI-Dengue is also implemented in the capital city of Porto Alegre, Rio Grande do Sul. Porto Alegre has a cooler and more subtropical climate than most of Brazil, and thus, has had a history of few dengue cases. For MI-Dengue, 712 traps were set in a grid across the city in October 2012, covering 44 km^2 with a trap density of 16 traps per 1 km^2. The dengue season started off uneventful with the IMFA index of vectors staying in the green range up until Week 44 of 2012 (the first week of November). However, in Week 47 an increase in vectors to an orange state of alert occurred, and dengue viral RNA was detected in mosquitos from four MosquiTraps, indicating the beginning of virus circulation in different areas of the city. This find was unusual for Porto Alegre, and a high alert of dengue risk was conveyed to the city. Since Porto Alegre does not have a history of indigenous dengue cases, and because it was also their first year using MI-Dengue, no chemical control was used and a mechanical approach of removing breeding sites was intensified.

The IMFA continued on into the critical red zone, and on Week 1 of 2013, the first indigenous human dengue case of the year was registered by the health department. However, the dengue cases did not end there. Week 4 of 2013 was characterized by another jump in IMFA to the critical red zone, and then on Week 8, four weeks later, a sustained peak of indigenous dengue cases was observed. At that time, Porto Alegre

began chemical control, and was able to partially suppress the vector population and prevent the cases of dengue from increasing further. Figure 7 shows the trends of vector population (IMFA), virus detected in mosquito (DENV), and indigenous human cases of dengue during this time.

In this scenario, MI-Dengue provided information about the risk of dengue outbreak seven weeks in advance of human cases. For vector control organizations in Brazil, having this information available ahead of time is causing a paradigm shift from reaction to prevention. Cities like Porto Alegre are learning the value of applying control based on detection of virus in mosquitos rather than waiting for dengue cases to appear in the human population. With each year, the cities are able to learn from the MI-Dengue data and optimize their control routine to best reduce the dengue burden for the population.

Cost-effectiveness

Each dengue epidemic causes an economic loss to both the government and population. Costs are incurred for hospital exams and treatment, as well as five to ten days lost from work for each dengue patient. To test the cost-effectiveness of the MI-Dengue system in preventing economic losses, a statistical study by the Colorado State University (CSU) was conducted analyzing the implementation of MI-Dengue in 21 cities in Minas Gerais over two years with an implementation cost of USD 0.54 per inhabitant per year. The results indicated that cities without MI-Dengue showed an increase in the number of dengue cases 2.7 times higher than cities with MI-Dengue between 2009 and 2010. It was estimated by the authors that in the year 2010, 27,191 cases of dengue were prevented, and with this, around $9 million dollars were saved by the Minas Gerais state government by using this Brazilian technology. The study also observed MI-Dengue to be most efficient in cities with developed economies and populations above 35,000 inhabitants, and the largest cost-benefit was found in cities with histories of high levels of dengue vector infestation and without close urban neighboring cities. This study shows that while dengue remains a large challenge in Brazil, there are opportunities to have a positive impact on controlling epidemics.

Future directions

With the information from MI-Dengue and MI Virus, Ecovec generates terabytes of data annually regarding the dengue vector population and viral circulation.

To learn from the past nine years of data and to better understand the complex transmission cycle of dengue, Ecovec plans to explore the possibility of using predictive models that incorporate many variables to better define the risk of dengue for a city at a given time. The predictive models to be explored will use vector density and viral circulation data generated with MI-Dengue and also may incorporate data regarding human movement and climate such as rainfall and temperature.

Modeling approaches for dengue risk prediction have been published academically with some success, but there is not yet available a commercial solution ready for implementation at the city level.

Ecovec hopes to develop a comprehensive solution for predictive modeling of the risk of dengue to be implemented in Brazilian cities and give city governments another tool to protect their population from the disease.

Figure 7: Vector infestation, viral circulation, and human cases of dengue are compared on this graph. An increase in vector infestation and viral circulation is closely followed by an increase in human cases of dengue.