The NSF Industry-University Center (I/UCRC) at FIU has developed tools and expertise to assist in operational and analytical health informatics. We propose leveraging the Center’s flagship project, the TerraFly Geospatial Analytics System, to provide applications in Dengue vaccine and disease management, including Dengue surveillance and Dengue vaccine evaluation and follow-up. TerraFly can also provide advancements for related applications in other areas of intelligent management of emerging diseases including Integrated Vector Management, vaccine management, cross-analysis of locations of patients and health providers and demographic and economic factors, and other geospatial and data-intensive applications. Using the existing technology developed under prior NSF funding, the Center would divide the incremental new application development costs between Sanofi Pasteur’s funding and the NSF AIR funding. The specific project proposed would provide a Historical Dengue Location-aggregate spatiotemporal application for Columbia and Brazil, design and prototype a system for in situ data collection at the time of vaccination, and integration of this into map-based efficacy analysis tools.

1. Background

According to the World Health Organization (WHO), vector-borne diseases are endemic in over 110 countries in the world and account for millions of deaths each year. Malaria alone, currently the most deadly vector-borne disease, accounts for over 1.2 million deaths per year, most of whom are children under the age of 5[1]. Health officials throughout the world are increasingly alarmed at the spread of the fastest growing vector-borne disease, Dengue. Dengue is a mosquito-borne disease caused by four types of dengue virus (types 1 to 4). These four Dengue viruses (DNV) causes disease that ranges from Dengue Fever (with or without warning signs) to severe dengue that can manifest as Dengue Hemorrhagic Fever and Dengue Shock Syndrome. It is estimated that over 2.5 billion people, or 40% of the world’s population, are at risk of contracting this serious disease, with an estimated 50 million infections and 400,000 cases of Dengue Hemorrhagic Fever each year. It is currently the leading cause of death for young children in several Asian countries [2;3].

To help overcome the devastating spread of Dengue, effective preventative measures are greatly needed. A vaccine to provide effective immunization from Dengue has the greatest promise to save countless lives. Vaccines have proven to be the most effective barrier available to prevent contraction of a disease [4]. Thus, the most effective means to stop the spread of Dengue is the creation of a safe and efficacious Dengue vaccine to immunize human populations, particularly those at highest risk. In the absence of the availability of vaccines for various vector-borne diseases such as Dengue, WHO has been advocating a policy of Integrated Vector Management (IVM). IVM is an evidence-based approach to intelligent planning, monitoring, evaluating and delivering vector-borne disease control measures that emphasize and integrate relationships between health and the environment, providing benefits to both [1;3;5]. Although the use of IVM has shown some positive results, much more work is needed. A more effective approach would use the positive results in IVM to support the development
and implementation of a Dengue vaccine. Effective implementation of the management of Dengue will involve a variety of approaches for rigorous and comprehensive surveillance, monitoring and evaluation of current and emerging data, including disease surveillance, vaccine evaluation and intervention impact monitoring and analysis. It also requires efficient and easy-to-understand means of dissemination and communication for mitigation and response to disease outbreaks [6].

To provide critically needed prevention and intervention measures against Dengue Viral illnesses, Sanofi Pasteur, the vaccines division of Sanofi, and one of the world’s largest companies specializing in the development of human vaccines, has created an investigational tetravalent dengue vaccine candidate to help fight spread of the disease. Sanofi Pasteur’s dengue vaccine, which targets all four virus types, has successfully passed Phase I, II clinical studies in adults and children in the U.S., Asia and Latin America. Currently, large scale Phase III dengue vaccine clinical studies in 31,000 adults and children are ongoing in Latin America (Mexico, Colombia, Honduras, Puerto Rico and Brazil) and in Asia (the Philippines, Vietnam, Malaysia, Indonesia, and Thailand).

Once Phase III clinical trials are completed and final approval is given, the immense effort of large-scale surveillance, effectiveness evaluation and worldwide distribution commences. To aid in this effort, researchers and healthcare providers will need robust, effective, easy to use tools that can quickly and easily provide up to date, detailed, location-based information on Dengue risks, outbreaks and vaccine outcomes for at-risk patients and geographic areas. The NSF I/UCRC at FIU propose to develop and provide advanced computing technologies that can significantly aid in this effort.

There are some existing tools that can aid in the critical types of surveillance, monitoring and analysis needed for effective immunization intervention against Dengue. One very powerful modality is the use of Geographic Information Systems (GIS). Geospatial and remotely-sensed data, such as georeferenced satellite imagery and aerial photography, combined with location-based map data, can provide particularly critical information that either is not available in other forms, or is not otherwise easily conveyed. Specifically, the monitoring and analysis of epidemiological data combined with geospatial data could provide a powerful analytics and easily understood visualization of results. A number of studies have documented the successful use of remotely sensed imaging technologies to track the environmental conditions that encourage the spread of malaria [8;9;10;11]. In these studies, predicted levels of malaria-vector mosquito populations based on remotely sensed imagery and GIS data approximated actual observed levels with upwards of 85% accuracy [12]. The analysis and visualization of geospatial remotely sensed and related data could also effectively be used for Dengue. For example, remotely sensed and GIS data could be used to predict the likelihood of a Dengue outbreak in particular areas given certain characteristics such as environmental factors and vaccine coverage. This would then lead to pinpointing the populations in most need of immediate immunization and intervention.

Implementing the cutting-edge technology needed for these types of solutions is complex and challenging. Massive amounts of data are required, and this data is often heterogeneous, from divergent sources, and consists of both structured and unstructured data. Further, the tools available for these types of analyses, and the expertise currently needed to use those tools, can be very costly and out of reach for many affected communities [13;14;15;16;17]. Many victims of Dengue are located in resource-poor areas. In addition, with these limited resources, communicating and improving adherence to the needed interventions is also a major challenge. This makes it a major task to find easy-to-use and cost-effective solutions that can help both local and international public health officials’ work towards implementing and maintaining a Dengue disease management program.


Combining epidemiological data with remotely sensed imagery and map data can enable public health workers and epidemiologists to more accurately engage in Dengue disease surveillance, identifying correlations between environmental and other risk-related data and the spread of Dengue. Further, this would improve our ability to identify areas in most critical need of additional surveillance and intervention. It would also enhance the ability to evaluate the efficacy of various interventions, such as the introduction and continued use of new preventative vaccines, the management of at-risk and affected populations, including patients and potential patients, and the coordination of medical providers. There is an advanced yet easy to use technological solution that can be implemented to...
further the types of monitoring and analyses needed in Dengue disease management and vaccine intervention. The needs of Dengue disease management are very similar to the needs in other types of disaster mitigation, and one GIS system that is designed for use in disaster mitigation, TerraFly, can provide a powerful solution to meet these needs. TerraFly is a solution that efficiently and effectively deals with the challenges involved in handling and analysis of massive amounts of heterogeneous geospatial and related data, as well as with the challenges that users encounter when attempting to use traditional GIS tools. Thus, we propose leveraging our TerraFly Geospatial Analytics System to create an advanced yet easy to use system for Sanofi Pasteur to aid researchers and healthcare workers in Dengue vaccine and disease management, including Dengue surveillance and Dengue vaccine evaluation and follow-up. As is discussed in more detail below, this system will employ advanced GIS technologies to provide detailed, location-based information that is critical to timely detection, intervention and analysis of Dengue risk factors, disease surveillance, vaccine distribution and outcome analyses.

TerraFly is a technology comprised of tools for visualization and querying of geospatial data. The visualization component of the system provides users with the experience of virtual "flight" over maps comprised of aerial and satellite imagery overlaid with geo-referenced data. The data drilling and querying component of the system allows the users to easily explore geospatial data, to create geospatial queries, and get instant answers supported by high-performance multidimensional search mechanisms. TerraFly's server farm ingests geo-locates, cleanses, mosaics, and cross-references over 40TB of basemap data and user-specific data streams. TerraFly's Application Programming Interface allows rapid deployment of interactive Web applications to provide customized, innovative solutions for many domains; it has been used to produce systems not only for disaster mitigation, but also for ecology, medical provider locating services, medical examiner data, crime, real estate, tourism, and municipal services. TerraFly's Web-based client interface is accessible from anywhere via any standard Web browser, with no client software to install.

TerraFly has been covered by both popular and specialized media, including TV (e.g. Fox and Discovery), radio (NPR), newspapers (e.g. New York Times, USA Today), magazines (e.g. Science) and journals (e.g. Nature). The project's primary sponsor is the National Science Foundation (NSF). Of the 53,000 NSF-funded projects in 2009, it chose 120, including TerraFly, for the NSF annual report to congress [18].

The TerraFly solution features portability, fly-over data-browsing technology, ability to integrate multiple sets of geospatial and local data into customizable, multi-layered products, and inclusion of powerful but easy to use visualization, querying and analysis tools. As can be seen on TerraFly's landing page (see Figure 1) [19], users are able to easily select and explore any geographic area of interest. By streaming incremental imagery tiles, TerraFly enables users to engage in virtual flights.
(see Figure 2) where they maintain full control over flight speed, direction and altitude (spatial resolutions) via an intuitive navigation system.

Unlike most GIS applications [20], TerraFly eliminates the need for the end-user to deal with any technical aspects of the system. The tools available in TerraFly include user-friendly geospatial querying, data drill-down, interfaces with real-time data suppliers, demographic analysis, annotation, route dissemination via autopilots, customizable applications, production of aerial atlases, and an application programming interface (API) for web sites.

Users are able to easily query for data of interest, and have that data automatically visualized in the form of non-obstructing geo-referenced overlays, or data layers, combined with spatial imagery [19; 20; 21; 22]. Any data capable of being geo-referenced can be input into TerraFly and overlaid onto spatial imagery. The most popular types of overlaid data include NAVTEQ NAVSTREETS street vectors, World OpenStreetMaps, property parcels, Yellow pages, White pages, demographics, and Worldwide Geographic places. In addition to data overlays, TerraFly provide users with a drill-down detailed information page on a point or area (see Figure 3). For example, users can use TerraFly to “fly” to a specified address, and then request more specific information about that particular location with a click of the mouse. A preview page will pop up in the flight window that contains a summary of information about that location, along with links to more detailed location information.

A critical component of TerraFly is its data repository, and a major strength lies in its integration of heterogeneous data sources including relational and semantic databases and web sources with spatial data. TerraFly’s data repository was one of the first GIS databases that were able to store heterogeneous data in one database [23;24;25;26;27;28]. As with other GIS tools, there are two main types of geo-referenced spatial data that TerraFly must handle: raster (satellite and aerial photography) and vector data (points, lines and polygons) [29]. TerraFly’s data repository currently stores over 40TB of geospatial and related data.
2.1. Advanced Data Visualization Capabilities

One of TerraFly’s cornerstone capabilities lies in its empowerment of its users. TerraFly provides robust systems and tools that are very flexible and easy to use, so that end-users can focus on the work that they need to get done without having to worry about the technology behind the system they are using. Even non-technical users are able to very quickly and easily create complex queries that combine heterogeneous data without requiring database expertise. For example, for effective vaccine management, more than surveillance and analysis to track and predict outbreaks of disease is needed. Appropriate and efficient planning and dissemination of preventative and intervention vaccines is also needed. TerraFly can provide easy-to-access tools to aid in the planning and coordination needed for this type of work.

TerraFly is able to easily combine complex, medical-related queries with geospatial data to provide users with information such as the location, distribution and density of medical clinics in relation to population, or any other information of interest. With a few clicks of the mouse, this information is presented to users in both visual and textual forms. An example of this can be seen in Figure 4, which visualizes the following query: “Where are all of the medical clinics that do not have backup clinics nearby and are located in middle income areas within densely populated sprawl.” This type of query could easily be changed to accommodate the user’s informational and analytical needs. It could, for example, help public health and other officials intelligently plan and coordinate the most effective interventions by looking at patient and population density combined with possible medical outreach location distribution.
Figure 4. All of the medical clinics that do not have backup clinics nearby and are located in middle income areas within densely populated sprawl.
A powerful capability of the system is the TerraFly TimeSeries application. This application has a unique ability to efficiently retrieve geospatial and remotely sensed imagery of the same geographic location that was acquired during different time periods. The system is then able to create an animated sequence over time to clearly show historical changes. The resulting time series can be quite dramatic and useful. This capability has been used in disaster mitigation, and can provide similar, powerful applications in Dengue vaccine management. For example, TerraFly could be used to monitor and understand changes in certain features or characteristics of a particular area that might be risk factors for Dengue, or be used to monitor the impact of the use of a preventative Dengue vaccine in known risk areas. Changes in levels of stagnant water, for instance, could be monitored and visualized over time, providing an easy to use method to discover areas at higher risk of Dengue outbreaks, and plan and coordinate vaccine interventions.

The recent earthquakes and tsunami that hit Japan in March of 2011 provides an example of the power of this technology. As can be seen in Figure 5, the before, during and after geospatial images, respectively, of the tsunami are quite dramatic. In the image from April 4th, 2010, entire neighborhoods can clearly been seen as having been established and intact. The image from March 12th, 2011, the day after the tsunami hit, shows that water has rushed well inland, inundating those neighborhoods. The final image, from March 19th, 2011, shows the aftermath once the waters have finally receded. Those neighborhoods were completely decimated.

TerraFly includes autopilot technology that allows users to preplan and map out a customized flight path of interest. With this tool, end users can quickly and easily select specific destinations, and the system will automatically create that flight path at the speed and altitude (resolution) desired at will by the user. The user is able to determine which features will be displayed while traveling in the flight path. In essence, any feature or information that is possible to view when the user is in manual mode can be added as a component of the requested flight path. For example, public health officials could create coordinated autopilot flight paths over specific areas of interest to aid in monitoring and analysis of Dengue disease spread. They would not have to manually control movement over the
area of interest and could, instead, just focus on gaining the information that they need. Further, this same flight path could easily be used over and over as updates and new information come in, and its path can be annotated with voice clips, images, and data. This would not only make it easier to manage Dengue vaccine interventions, it would also aid in more effective and accurate communication with healthcare workers as each individual could be provided with his or her own preconstructed autopilot path instead of trying to describe areas of interest in a verbal or text-based manner.

Figure 6. In situ data and graphs in TerraFly for Use in Hydrological Analysis

TerraFly also provides numerous data analysis and visualization tools for scientists in various domains. Figure 6 shows Hydrology data analysis tools in TerraFly. With this tool's intuitive interface, users are able to view and analyze data, and have results of their analyses displayed as imagery, charts and tables. Additional functionality found in TerraFly, such as time series data, key word searches, and layer control, is also available on this screen. For example, users are able to select a date range and view time series animation of changes, as well as graphs that plot these changes over time. As can be seen in Figure 7, very detailed geospatial temporal plots are available to users of this application. As with all TerraFly flight windows, locations are searchable by address, and more detailed data for specific points is available at the click of the mouse. For example, clicking on one of the stations provides information about that particular site. With TerraFly’s flexible technology, interfaces and analytical capabilities can easily be customized for specific uses for Dengue disease and vaccination analysis and management.
There are also numerous capabilities in TerraFly that individuals find useful in their day-to-day lives that could be useful for public health officials. Overlaying data from the White Pages, for example, improves its usability for many individuals (see Figure 8). Users are able to search for needed information in the White Pages not just by a person’s full name, but also by attributes such as address, phone number, or the names of other individuals in the home. Alternately, users can search the geospatial imagery visually to find a particular location, and related information. This can easily be tailored to the information that is available in specific areas or countries, and can be particularly useful for public healthcare workers and researchers who are in need to more detailed, personalized information on potential disease impact on individuals or targeted populations. For example, assuming the data is available, these capabilities can help fine tune predictive models and impact analytics by finding and focusing on areas that have large populations of high-risk individuals, such as children under 5 years of age.

2.2 Dengue project for Sanofi Pasteur
The specific proposed project for Sanofi Pasteur is comprised of:

**A. Historical Dengue Location-aggregate spatiotemporal application for Columbia and Brazil.** A first partial prototype of this application is:


**B. Design and prototype a system for in situ data collection at the time of vaccination and integration thereof into map-based efficacy analysis tools.** The eventual system will allow real time data collection at the time of vaccination via a survey technology and real time integration of this data into analytical and efficacy map-based tools. In the proposed project, the system will be designed, the data simulated, and a prototype map-based application will be developed. The data collection design will be based on LOCWORLD GEO-DYNAMIC MOBILE: Mobile Geo Collection of Field Survey Data

This is a mobile application, running on a low-cost cellphone, for field collection of a very wide range of information, including automatic geo-referencing. One of the main problems in collecting and processing any type of information in the field is the long and complicated process of data entry. Traditionally, surveyors had to collect information using pen and paper and afterwards tabulate the results for later analysis.

Organizations collecting field data cannot afford the costs of developing customized mobile applications to their specific needs. The LocWorld platform dynamically generates mobile applications for agencies involved in activities that require field data gathering. With LocWorld Geo-Dynamic Mobile applications, collecting field survey data in Latin America becomes a fast, productive and efficient process.
Benefits:

- Increase effectiveness of field data collection with tools that allow surveyors to collect any type of data with their cellphone.
- Eliminate costs and time associated with tabulating data twice; optimize data summary and analysis.
- Create dynamic surveys and campaigns adapted to meet specific needs, and compile data automatically in record time.
- Rely on automatic reports that enhance geo-analytical capabilities and promote effective decision-making.
- Optimize processes and reduce operating costs.

How does LocWorld do this?

- LocWorld integrates advanced technological tools (Web, Cellular, GPS, Digital Mapping, etc.) into a comprehensive solution that optimizes automatic field data collection which also reduces user data entry errors.
- Surveys are easily generated by or for any kind of company, whether small, medium, large, corporate, private or public.
- This LocWorld Dynamic Survey Solution has two components:
  - A Mobile Application Generator – a Web-based interface for the generation of unlimited mobile survey applications
  - Mobile Applications

How does Geo-Dynamic work?

- Any authorized executive, from any place in the world, using a Web-based interface, creates a survey or form an App.
- Automatically sync the newly created survey or form App with any number of mobile phones to summarize the collected data.
- Gather field data anytime, anywhere in Latin America.
- Easy data entry on site.
- Automatic geo-referencing using cellphone GPS and/or triangulation.
- Photograph entry.
- Voice/transcription text.
- Visualize, centralize or distribute the collected data in reports generated by the web application, with sophisticated location data analysis tools.
- Get immediate information for rapid solutions and health interventions.
2.3 Summary

Through the implementation of innovative techniques and technologies, TerraFly provides users with GIS capabilities without the need to learn complex interfaces or deal with the technology behind the system. It is a robust, user-friendly system that has wide appeal to many different types of users, and application to many different domains. The use of TerraFly in Dengue surveillance, intervention evaluation and follow-up, such as managing and analyzing vaccine coverage and impact, could provide public health officials and researchers with critical analysis and visualization tools that they otherwise would not have access to. It could also provide public health officials and researchers with powerful tools to improve the ability to quickly and easily communicate critical information in a visual format. This will increase our capabilities to mitigate, and eventually eradicate, the Dengue disease.

Contact

Naphtali David Rishe, Ph.D.
Professor, School of Computing and Information Sciences
The inaugural Outstanding University Professor
Director, High Performance Database Research Center
Director, NSF Industry-University Cooperative Research Center at FIU, FAU, and Dubna U
Director, NSF Center of Research Excellence in Science and Technology at FIU
Director, NASA Regional Applications Center in Miami
Florida International University
University Park, ECS-243, Miami, FL 33199
Direct: (305)672-6471; Secretary: (305)348-1706; Fax: (305)348-1707
rishe@fiu.edu skype:ndrishe http://cake.fiu.edu/Rishe http://TerraFly.FIU.edu

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