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Real-Time, Autonomous Biosurveillance for Vector-Borne Viral Pathogens

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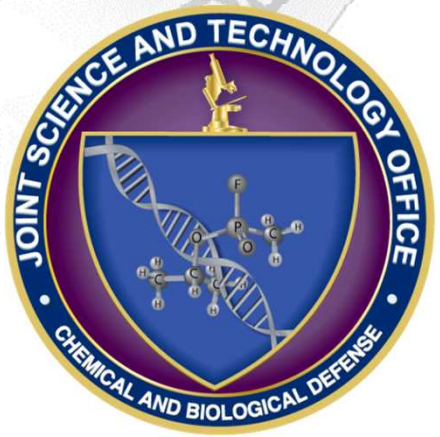

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Project Overview

- Develop and field-test an *autonomous sensor* to detect presence of mosquito-borne viruses (West Nile, etc) with daily reporting
- Integrate sensor data into BSVE along with mapping & visualization software and predictive models.
- 3-year effort began 2014 (~16 months in)
- Partnership between Sandia National Laboratories (Livermore)
  - Systems engineering, microfluidic assays, statistical modeling
- …and UC Davis Center for Vectorborne Diseases (CVEC)
  - Virology, entomology, and ecology of vectorborne disease
  - Integrated with public health and vector control districts in CA

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Why arboviruses?

- "Arbovirus" = Arthropod-borne virus
  - Mostly RNA viruses; carried by mosquitoes, ticks, flies, *etc*
- West Nile swept the globe in a few years – what's the next epidemic to emerge?
- Threat to military personnel overseas.

Dengue
Yellow fever
Chikungunya

West Nile virus*
St. Louis encephalitis virus*
Japanese encephalitis virus
Rift Valley fever virus
Equine encephalitis viruses
(WEE*, VEE, EEE)

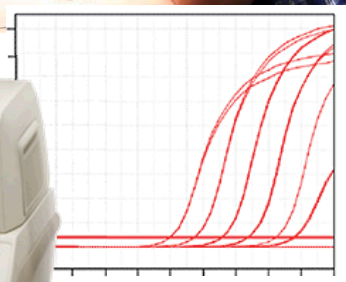
Transmits malaria
(not a virus!)

Ground truth for arboviruses

Vector surveillance

Photo: Fairfax County, VA via Flickr


Photo: Palm Beach Post



Molecular assays

~2 weeks

Adulticide spraying

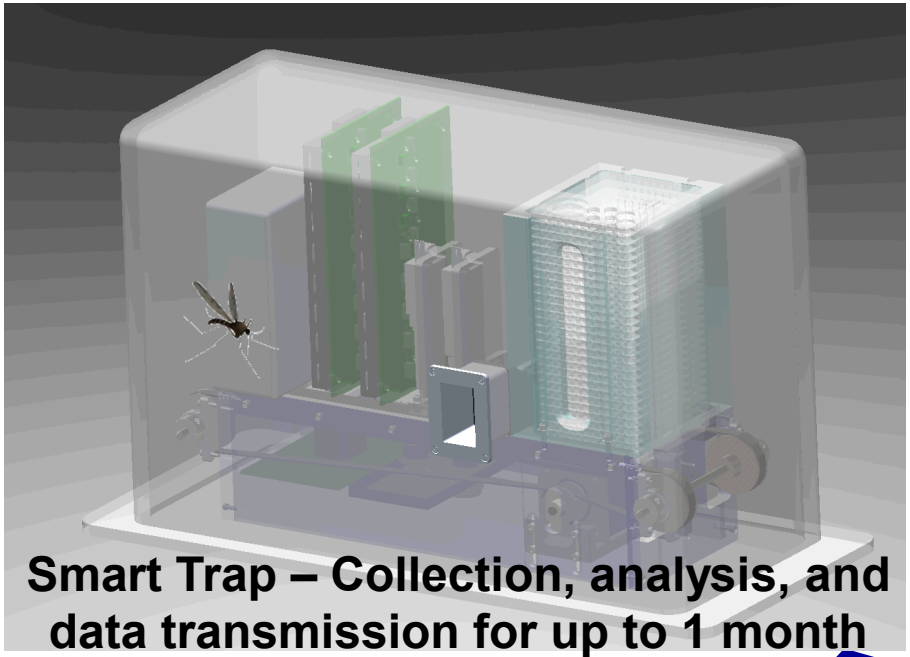

Photo: Huffington Post Alamy


Photo: Lafayette City Parish Gov

Sugar-based surveillance

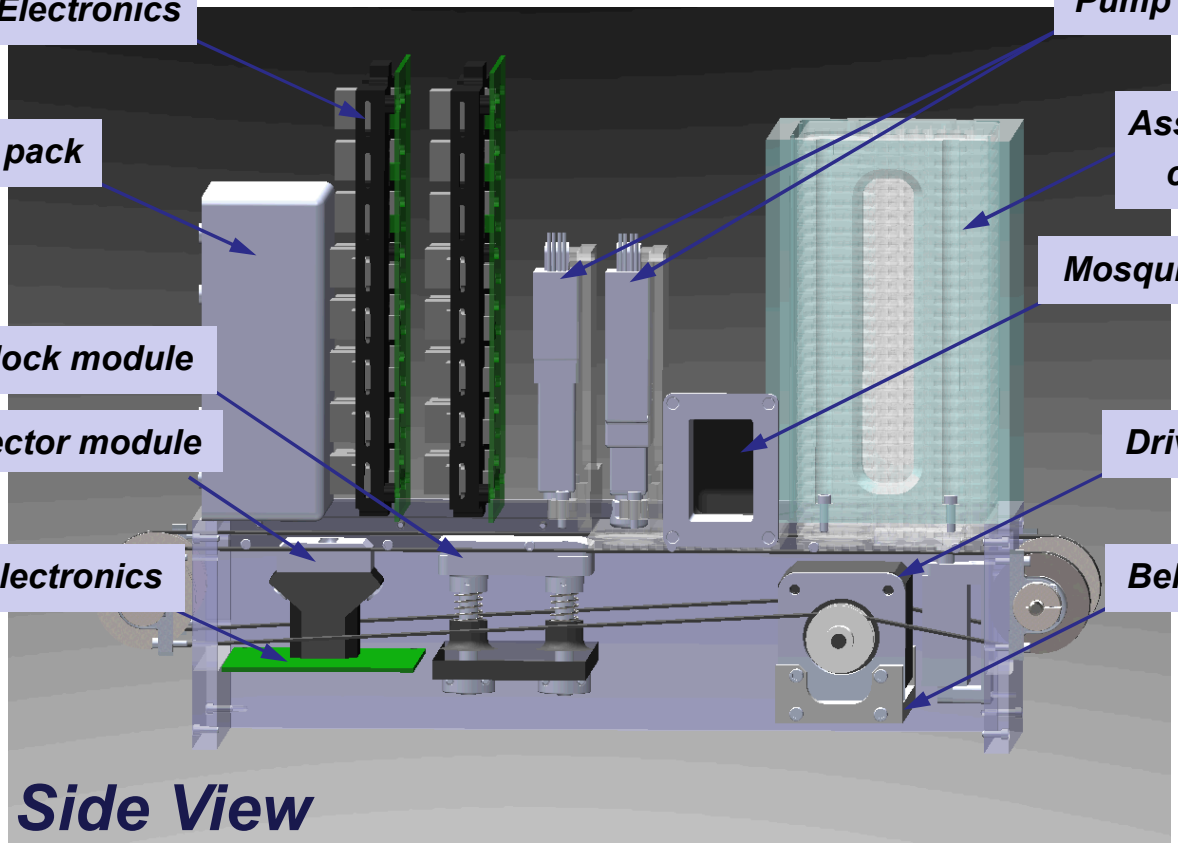
- Besides blood, mosquitoes feed on sugar for energy.
- Infected mosquitoes deposit virus while sugar-feeding.
- We propose to exploit sugar-feeding in an *autonomous field-based detector:* the **Smart Trap**
- Needs to do a complex job, but be cheap enough to deploy in a network for spatial surveillance

Sugar baits used for field collection followed by laboratory analysis



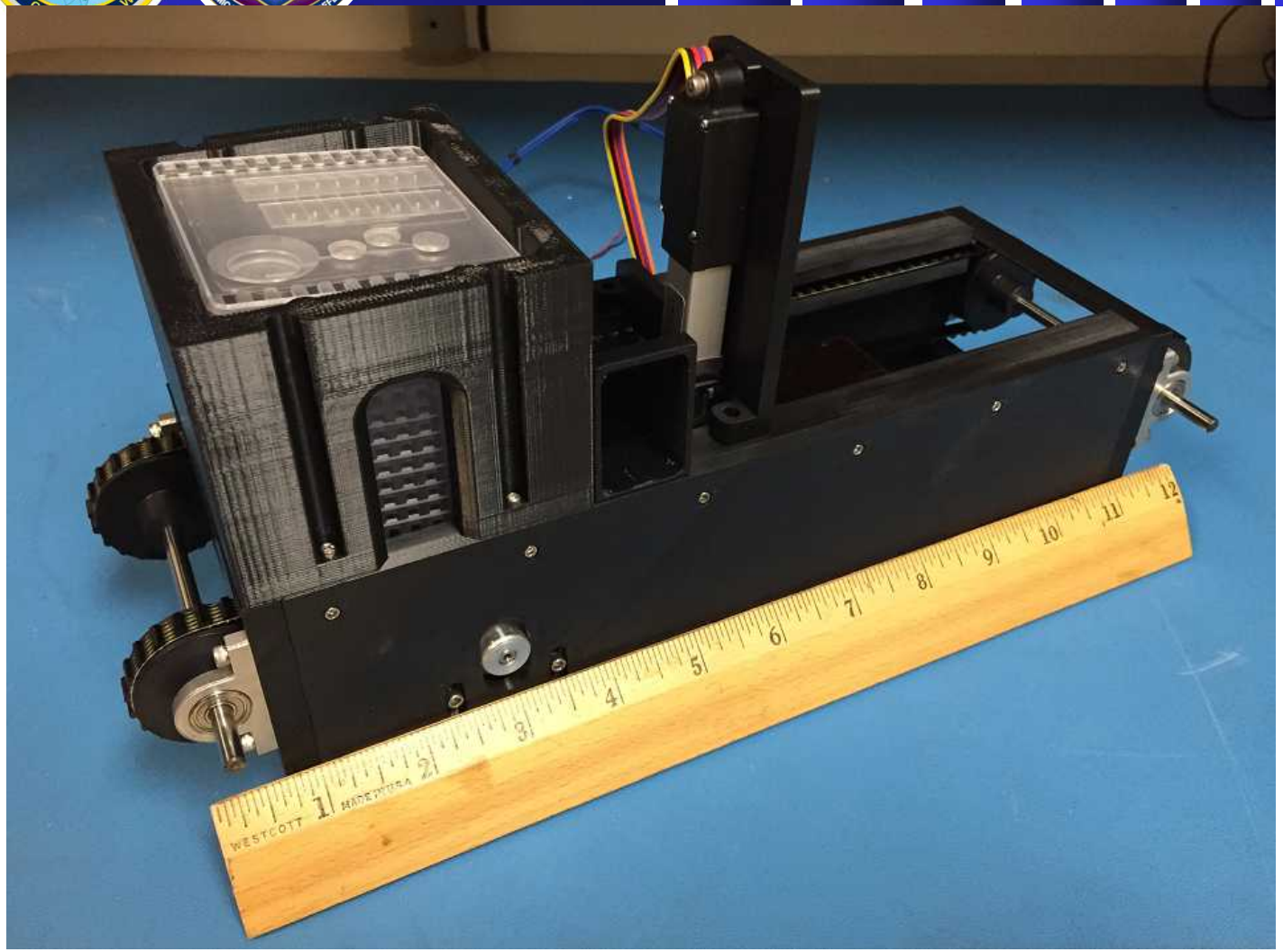
Smart Trap – Collection, analysis, and data transmission for up to 1 month

Smart Trap Concept



System cover and side covers removed for illustration purposes

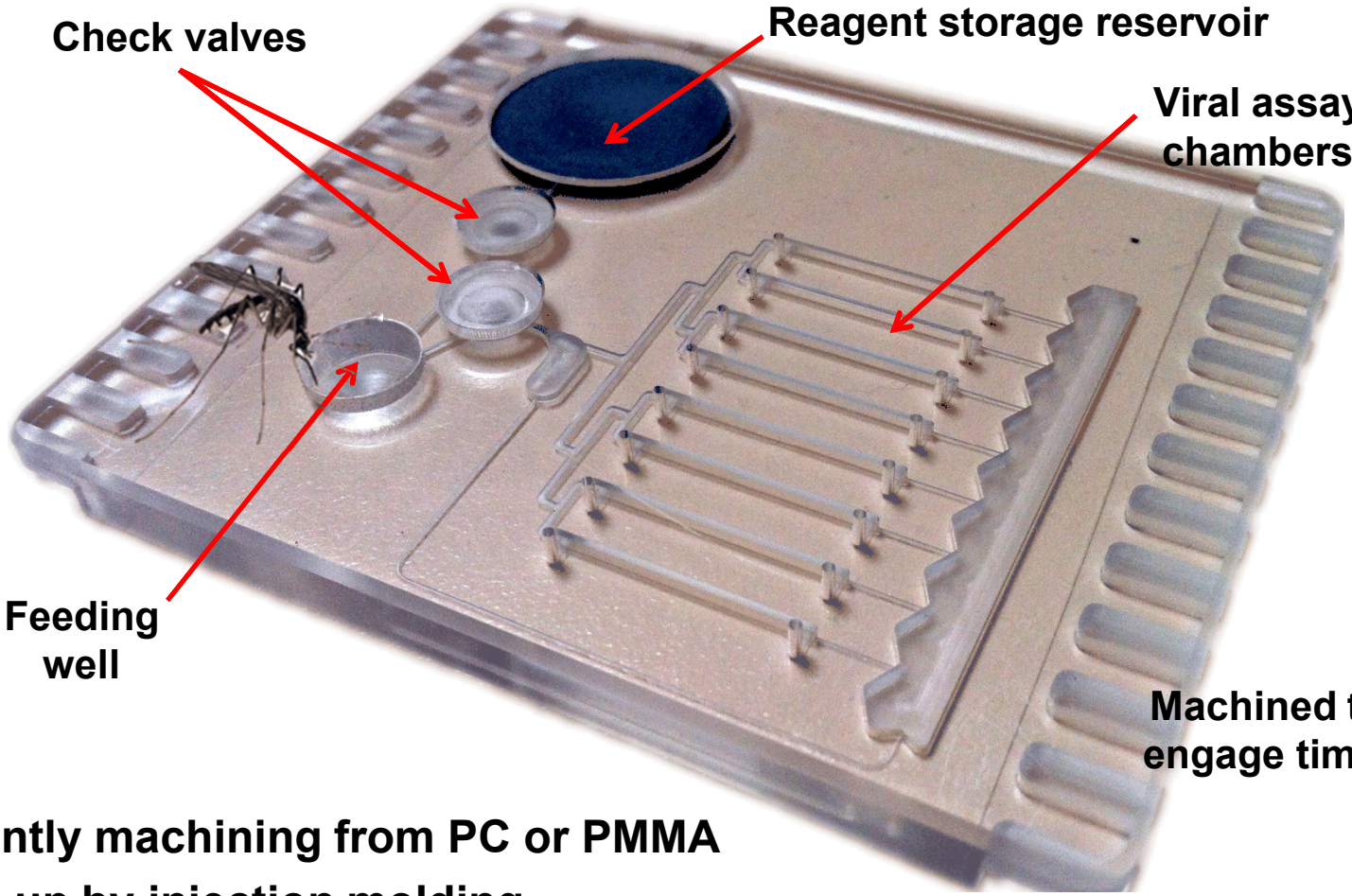
Smart Trap Prototype



Approximate size : 14 x 6 x 8 inches

R.F.Renzi 02/2015

Daily assay cartridge

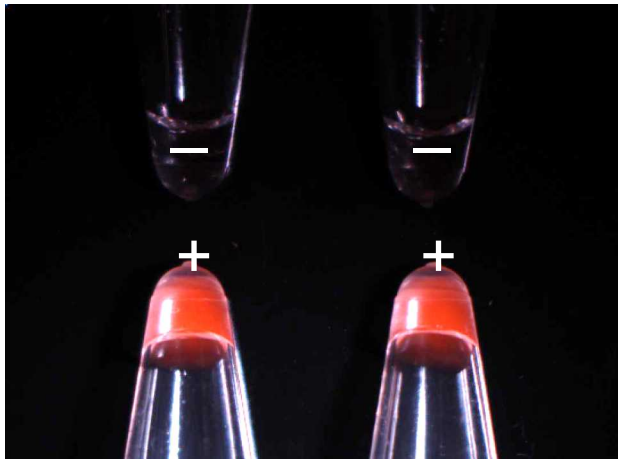


- Currently machining from PC or PMMA
- Scale-up by injection molding

Viral assays by RT-LAMP

- Isothermal amplification of viral RNA (63 °C)
- Requires minimal sample prep / RNA extraction not necessary
- Detects <0.1 PFU virus in ~30 minutes
- Created novel primer sets for WEEV and SLEV
- Novel Sandia-developed detection chemistry gives bright and distinctive fluorescence endpoint signal

WNV RT-LAMP endpoint

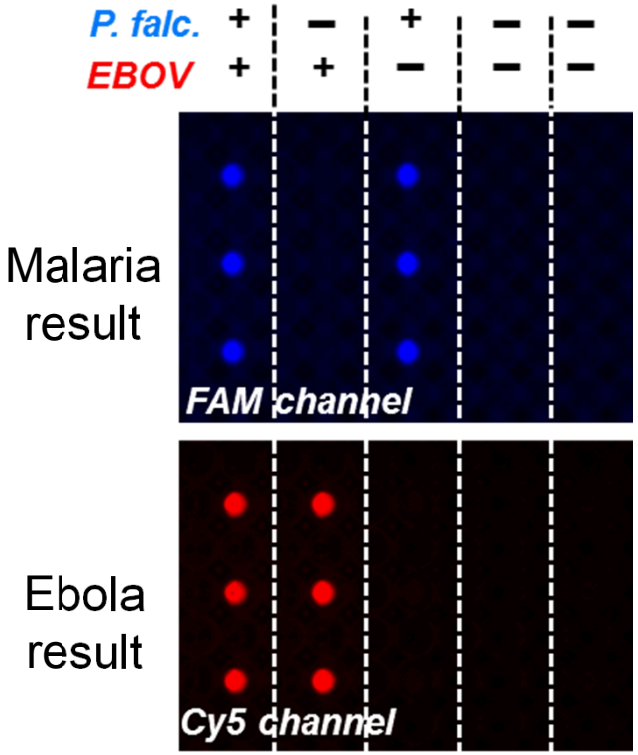


Implemented in Smart trap with a simple LED and photodiode detector

Also works with an LED flashlight and a color camera (*e.g.* smart phone) with a red plastic film as an emission filter.

Potential for clinical diagnostic

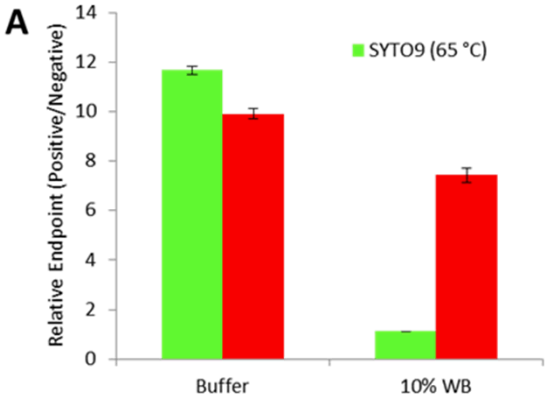
Single-tube multiplexing Ebola and *Plasmodium*



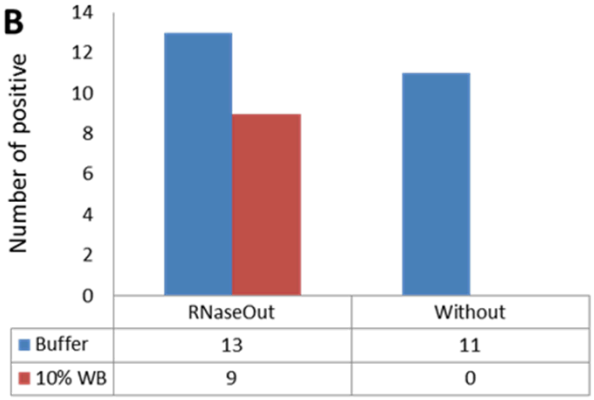
Adaptable to bright visual readout

Newly designed RT-LAMP primers for Ebola GP gene target both historic (1976) and recent (2014) isolates; detect 200 copies in about 20 minutes

RT-LAMP with new detection technique enables detection of Ebola RNA directly in whole blood (10% of total reaction volume, no RNA extraction)



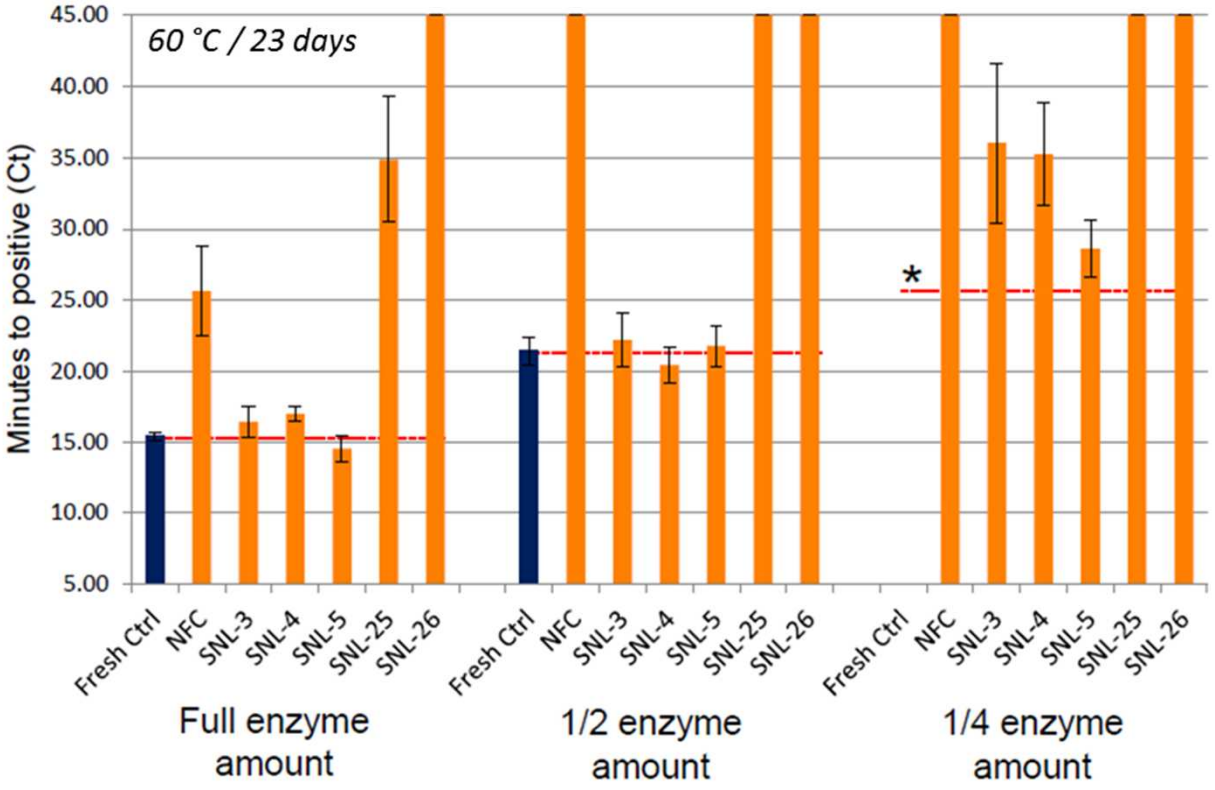
1000 copies EBOV RNA
(100% detection rate)



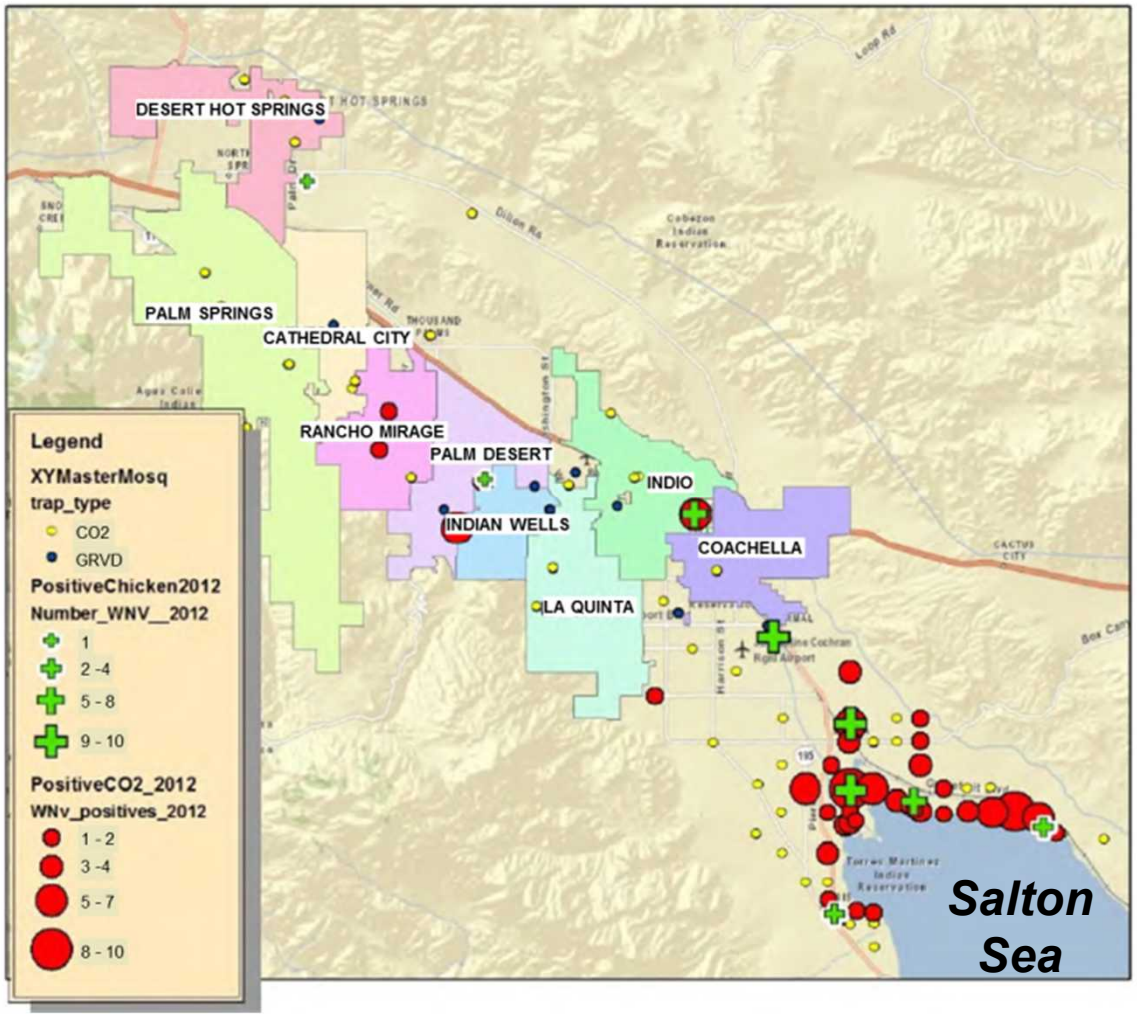
200 copies EBOV RNA ×
20 replicates per condition
~50% detection rate

Field stabilized reagents

- Partnered with Biomatrica to formulate RT-LAMP assay reagents for long-term stability in dry form in assay chip; rehydrate with “bait fluid” to run assay.
- Minimal loss in activity after >3 weeks at 60 C, even with reduced enzyme



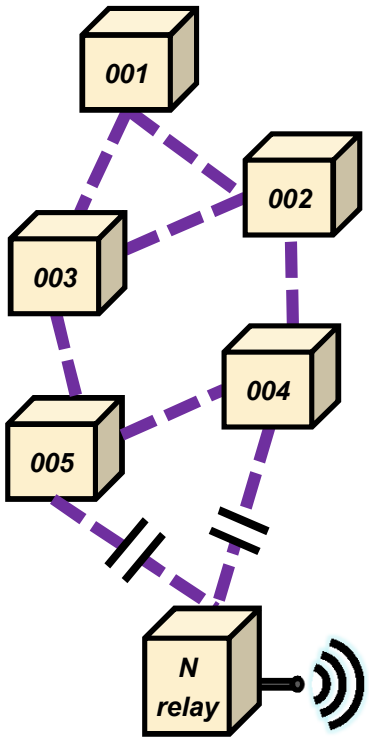
Field test planned 2016



- Will deploy Smart Trap network near Salton Sea
- Perform field test concurrently with conventional vector surveillance for WNV (traps & sentinel chickens)

Trap wireless networking

Private wireless trap network



Cellular-enabled relay node

SMS-coded "result" messages

001A%k…

002z4m…

*003B*r…*

004ybA…

005xcD…

NNNj#z…

Translate results using BSVE PON diagnostic XML schema

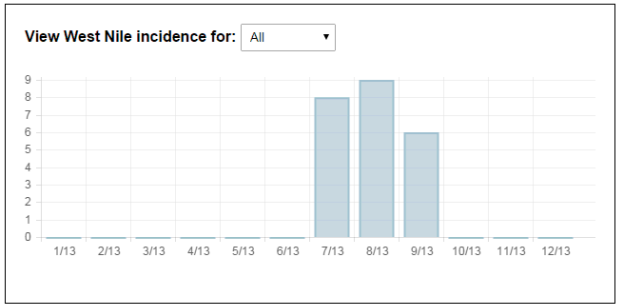
Receiver
cellular / cloud

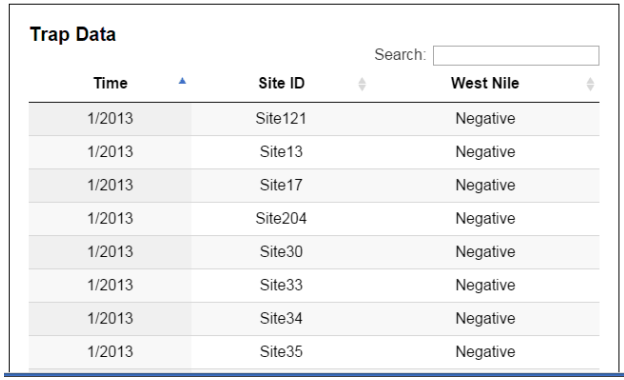
AWS Cloud
Trap data
Maps
Model predictions

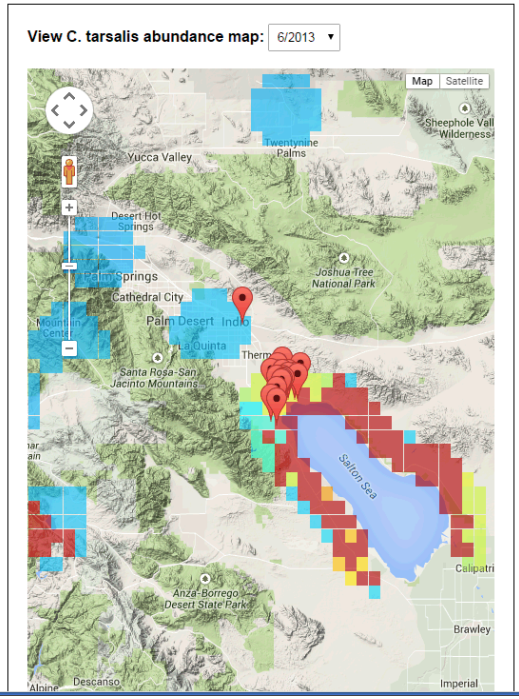
BSVE

AWS screenshot

- Trap data stored using PON diagnostic XML schema
- Trap data viewable as time series, or search by location & date
- Behind the scenes: CA vector control data, environmental data, trap data, and statistical model (R script) produce vector abundance map and infection rate map
- Model is anchored at trap locations; interpolates through space

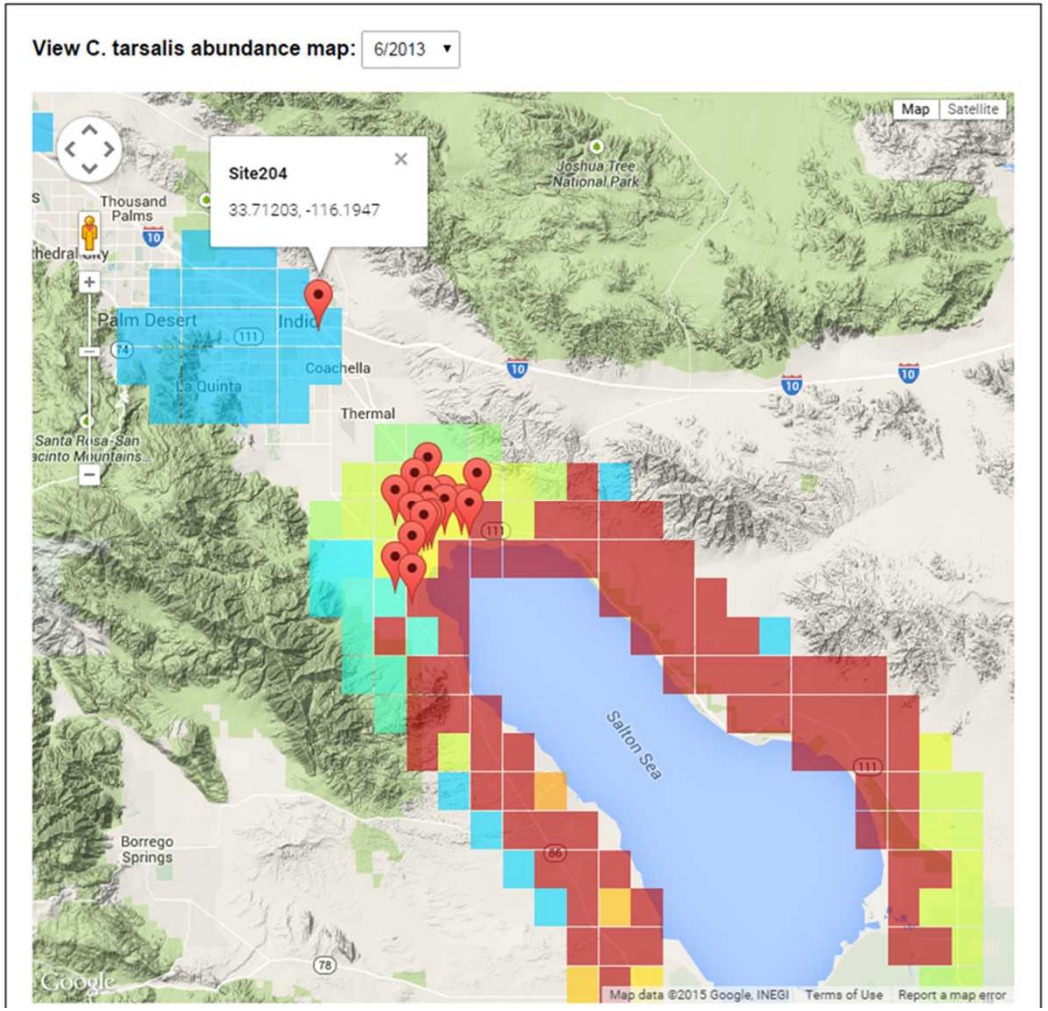






AWS site visualizations

- Pushpins at trap locations
- Model predictions overlayed on map
- Map results selectable by date



Future prospects

- Just beginning year 2 of 3-year Smart Trap effort
- Maturing hardware & field testing components
- How to attract the most mosquitoes?
- Correlating sugar-feeding to conventional trapping & surveillance
- Adapting to other targets
  - Other viruses (Dengue, chikungunya, JEV, etc)
  - Plasmodium parasites
  - Other arthropod vectors: flies, ticks, etc?
- RT-LAMP / LAMP assay useful for simple yet sensitive PON test
  - human/veterinary use
  - virus, bacteria, parasite, drug resistance/virulence genes
  - Compatible with blood, saliva, urine, stool, etc.
  - Stabilization without cold chain