



# Ebola response in Liberia: A step towards real-time epidemic science

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<http://www.vbi.vt.edu/ndssl>





# Goals for today's webinar

- Want to introduce the population modeling working group to IMAG and invite you to be a part of the WG
- Describe efforts by two teams (Yale and Virginia Tech) to support Ebola response
- Introduce the use and role of multi-scale population modeling in computational epidemiology



# Team

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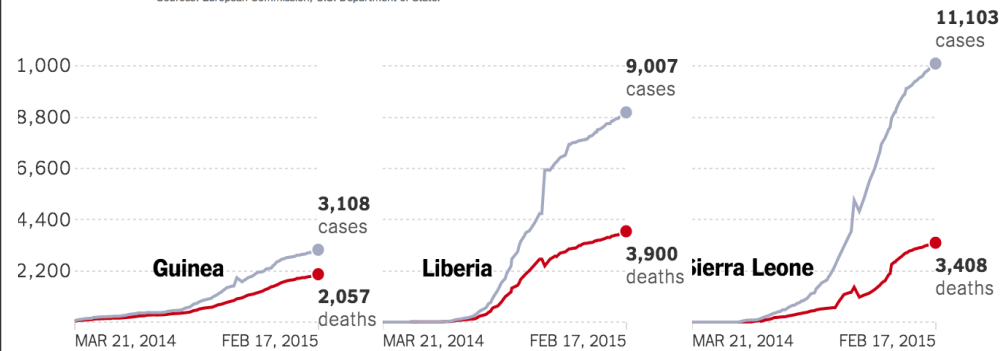
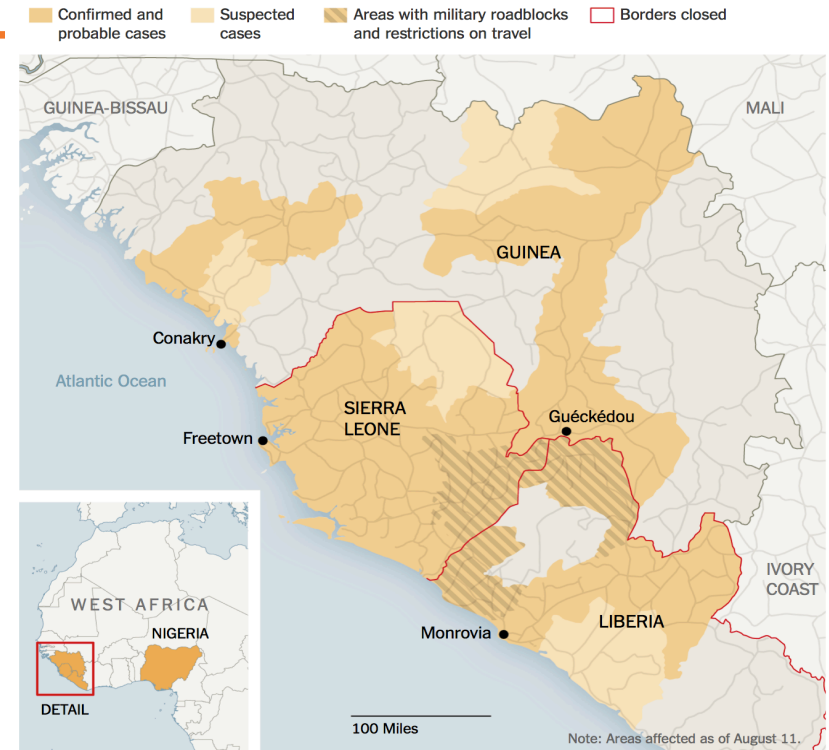
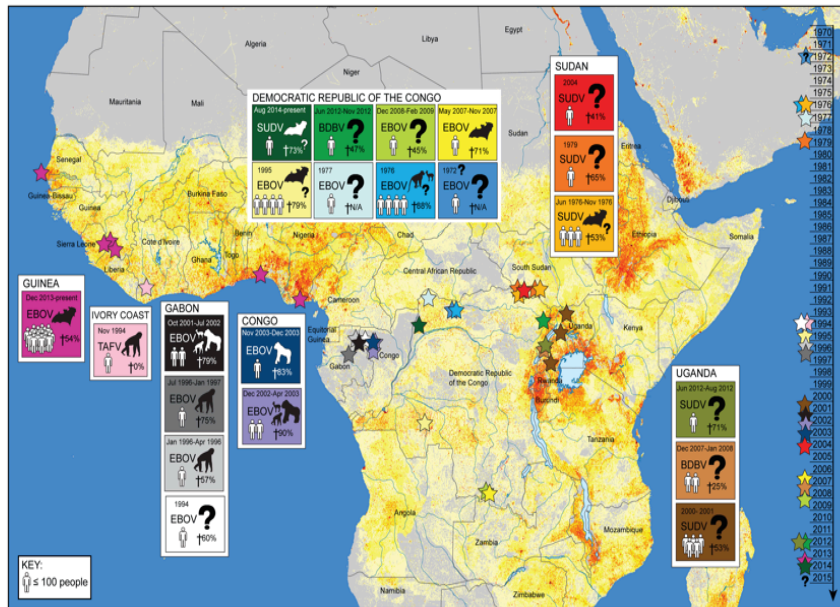
# Acknowledgements

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# Ebola outbreak in Africa

- Largest Ebola outbreak yet: 5 countries; 24000 cases; 9000 deaths.
- Excellent NY Times webpage: <http://www.nytimes.com/interactive/2014/07/31/world/africa/ebola-virus-outbreak-ga.html>



Note: The number of deaths and cases reported by the World Health Organization sometimes decreases because of data revisions.

Network Dynamics &amp; Simulation Science Laboratory



# Goal: Real-time response

EDITORIAL

- Before an epidemic
  - (i) Determine the (non)medical interventions required, (ii) feasibility of containment, (iii) optimal size of stockpile, (iv) best use of pharmaceuticals once a pandemic begins
- During an epidemic
  - (i) Quantifying transmission parameters, (ii) Interpreting real-time epidemiological trends, and (iii) assessing impact of interventions.



Harvey V. Fineberg is president of the Institute of Medicine.



Mary Elizabeth Wilson is associate professor of Global Health and Population at the Harvard School of Public Health and associate clinical professor at Harvard Medical School, Boston, MA.

## Epidemic Science in Real Time

FEW SITUATIONS MORE DRAMATICALLY ILLUSTRATE THE SALIENCE OF SCIENCE TO POLICY THAN AN epidemic. The relevant science takes place rapidly and continually, in the laboratory, clinic, and community. In facing the current swine flu (H1N1 influenza) outbreak, the world has benefited from research investment over many years, as well as from preparedness exercises and planning in many countries. The global public health enterprise has been tempered by the outbreak of severe acute respiratory syndrome (SARS) in 2002–2003, the ongoing threat of highly pathogenic avian flu, and concerns over bioterrorism. Researchers and other experts are now able to make vital contributions in real time. By conducting the right science and communicating expert judgment, scientists can enable policies to be adjusted appropriately as an epidemic scenario unfolds.

In the past, scientists and policy-makers have often failed to take advantage of the opportunity to learn and adjust policy in real time. In 1976, for example, in response to a swine flu outbreak at Fort Dix, New Jersey, a decision was made to mount a nationwide immunization program against this virus because it was deemed similar to that responsible for the 1918–1919 flu pandemic. Immunizations were initiated months later despite the fact that not a single related case of infection had appeared by that time elsewhere in the United States or the world ([www.ion.edu/swinefluaffair](http://www.ion.edu/swinefluaffair)). Decision-makers failed to take seriously a key question: What additional information could lead to a different course of action? The answer is precisely what should drive a research agenda in real time today.

In the face of a threatened pandemic, policy-makers will want real-time answers in at least five areas where science can help: pandemic risk, vulnerable populations, available interventions, implementation possibilities and pitfalls, and public understanding. Pandemic risk, for example, entails both spread and severity. In the current H1N1 influenza outbreak, the causative virus and its genetic sequence were identified in a matter of days. Within a couple of weeks, an international consortium of investigators developed preliminary assessments of cases and mortality based on epidemic modeling.\*

Specific genetic markers on flu viruses have been associated with more severe outbreaks. But virulence is an incompletely understood function of host-pathogen interaction, and the absence of a known marker in the current H1N1 virus does not mean it will remain relatively benign. It may mutate or acquire new genetic material. Thus, ongoing, refined estimates of its pandemic potential will benefit from tracking epidemiological patterns in the field and viral mutations in the laboratory. If epidemic models suggest that more precise estimates on specific elements such as attack rate, case fatality rate, or duration of viral shedding will be pivotal for projecting pandemic potential, then these measurements deserve special attention. Even when more is learned, a degree of uncertainty will persist, and scientists have the responsibility to accurately convey the extent of and change in scientific uncertainty as new information emerges.

A range of laboratory, epidemiologic, and social science research will similarly be required to provide answers about vulnerable populations; interventions to prevent, treat, and mitigate disease and other consequences of a pandemic; and ways of achieving public understanding that avoid both over- and underreaction. Also, we know from past experience that planning for the implementation of such projects has often been inadequate. For example, if the United States decides to immunize twice the number of people in half the usual time, are the existing channels of vaccine distribution and administration up to the task? On a global scale, making the rapid availability and administration of vaccine possible is an order of magnitude more daunting.

Scientists and other flu experts in the United States and around the world have much to occupy their attention. Time and resources are limited, however, and leaders in government agencies will need to ensure that the most consequential scientific questions are answered. In the meantime, scientists can discourage irrational policies, such as the banning of pork imports, and in the face of a threatened pandemic, energetically pursue science in real time.

— Harvey V. Fineberg and Mary Elizabeth Wilson

10.1126/science.1176297

\*C. Fraser et al., *Science* 11 May 2009 (10.1126/science.1176062).





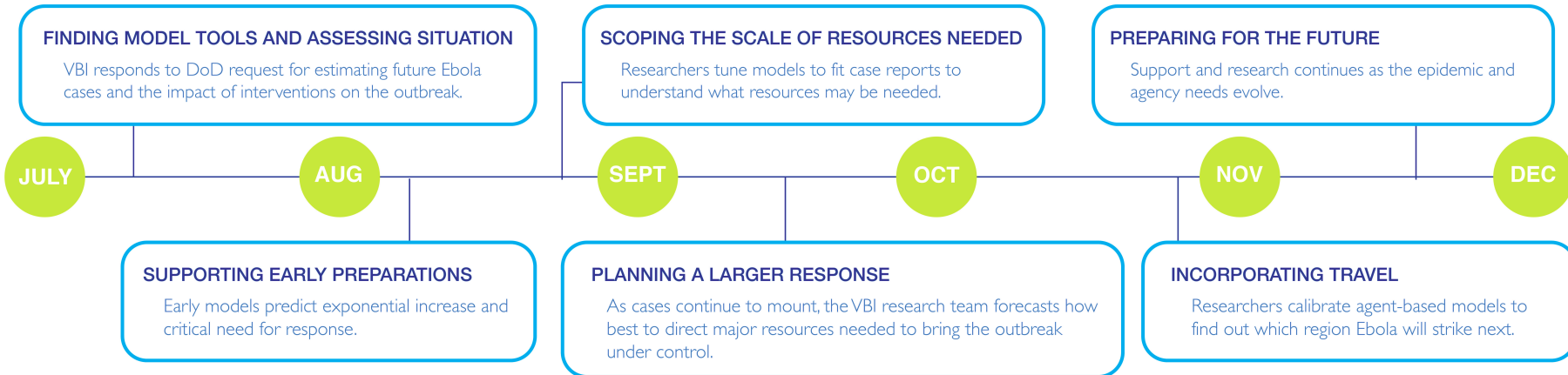
# Our approach: Informatics for integrated reasoning about situations and actions

- Goal: Build a suite of informatics tools that
  - Synthesize: available data to produce consistent and meaningful representation of the underlying system
  - Provide: range of interpretations of incoming measurements
  - Evaluate: range of response actions and behaviors
  - Monitor: Effect of policy responses evaluation of objectives
- Support coordination among diverse stakeholders
- Want to go beyond prediction
- Build systems, synthesize data and refine as we go along
  - Systems should be useable by analysts and not just by computing experts



# Response: Analysis and tools

## ► Our Response Timeline



30  
Presentations

1000+  
Slides

7  
Months of  
weekly  
engagement

6+  
Case studies

4  
Additional  
requests

5  
Countries  
Synthetic  
populations &  
networks

20+  
Press articles,  
interviews,  
papers

3  
New apps



URL: <https://www.vbi.vt.edu/ndssl/featured-projects/ebola>

## Our Ebola Research

### Summary

- Modeling Updates
- Resources
- Collaborations
- Funding
- Blog
- Publications

### Contact

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## Informatics Resources for Ebola Epidemic Response

### About Ebola

The latest Ebola outbreak in Western Africa has illuminated the significant threat posed by infectious diseases to human lives and society. The ongoing Ebola outbreak is by far the largest in history. As of October 12, 2014, over 5500 individuals have been confirmed infected and have caused almost 4500 deaths. It has ravaged Guinea, Liberia, Sierra Leone, with smaller outbreaks in Nigeria and Senegal, causing significant social, health and economic impact.

Ebola is a challenging disease to combat. There is no known cure and the mortality rate is high. While its origins are zoonotic in nature, once spread to humans, Ebola can be passed onto another through bodily fluids. The average incubation period is six days, but can last as long as 21 days. During that time, those that are infected are not contagious. However, given the means of transmission, the outbreak can be controlled using proper precautions.

The current web page is created so as to make the data, methods and analysis available to the world community in an attempt to speed up the scientific progress on this important public health crisis.

### Synthetic Information

-  [Sierra Leone](#)
-  [Liberia](#)
-  [Guinea](#)
-  [Nigeria](#)

[SI Visualizer](#)

### Ebola in the News

October 27, 2014  
[Quartz features Madhav Marathe; crowdsourcing and supercomputing and Ebola](#)

October 27, 2014  
[NDSSL's Ebola data and Hackathon featured in IBM Smarter Planet Blog](#)



# Examples of analytic support for Ebola response

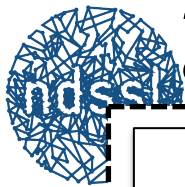
- *Estimating* basic epidemiological parameters for the outbreak
- *Forecasting* the ongoing epidemic with & without control
- *Assessing* the threat of imported cases in the United States causing secondary infections
- *Efficiently allocating* of potential pharmaceutical treatments
- *Location of Emergency treatment centers* and assessing the impact these centers will have on the outbreak
- *Estimating* the need for supplies such as personal protective equipment
- Analyzing Twitter data to assess public mood & sentiments
- Assessing the potential spread of Ebola to Latin American countries



# Lessons learned

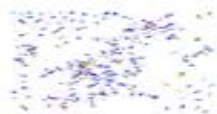
- Close coordination with analysts and policy makers is critical
  - Helped with problem formulations
  - Led to relevant analysis
  - Led to entirely new research questions and requirements
- Well trained multi-disciplinary team critical
  - Past experiences (e.g. SLE exercises, H1N1 response) allowed the team to be prepared and trained
  - Strong collegiality within the team as well as with DTRA, BARDA, NIH MIDAS and other groups was the key
  - Maintaining a ready team is important - cannot be assembled real-time
- Managing expectations: balancing science and timely response
  - Science is inherently a slow deliberate process, policy makers need results quickly and adaptively
- Utility of the tools developed to support the next epidemic outbreak





# SIMDEMICS: A comprehensive Cyber-infrastructure for computational epidemiology

Digital Library



Networks

Results

User Applications

EpiCaster

DISimS



EpiViewer

Game Apps



MY4Sight

FluCaster



Simfrastructure:  
Middleware to  
support pervasive  
app ecosystem

Models

Simulations

Forecasting

Analysis

Diseases

Compute Resources

HPC Cluster

Individual Server





# Pervasive webapps to support Ebola response

<http://www.vbi.vt.edu/ndssl/tools>



## EpiCaster

### EpiCaster

Users can view Ebola (or Flu) activity for the past four weeks and view forecast predictions for the next two weeks. They can also view forecast trends and compare them to surveillance data. EpiCaster allows users to see what impact various strategies, such as vaccines and social distancing, have on disease spread.



## EpiViewer

### EpiViewer

EpiViewer is a data repository for epidemiologists. Users can upload and compare Ebola forecasts and surveillance data from a variety of sources and see how forecasts change over time. Users can also load and share their own forecasting predictions.



## Eyes on the Ground

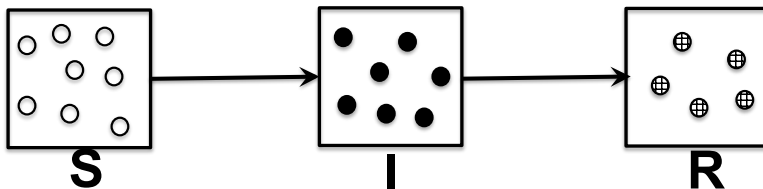
### Eyes on the Ground

Road conditions can be variable in some of the rural areas in Western Africa. Eyes on the Ground allows people in affected areas to report their road conditions. Other travelers can then view these reports and plan their trips accordingly. This is especially useful when planning the delivery of patients and supplies between cities.

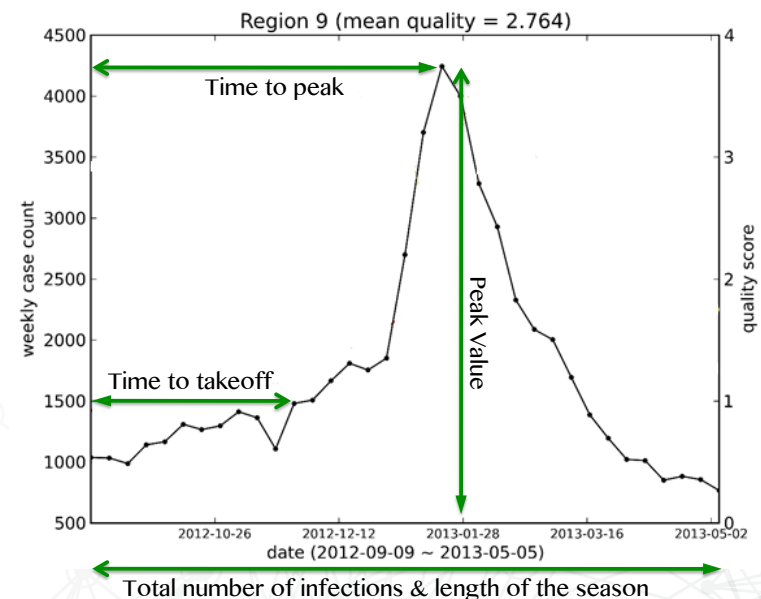


# Mass action compartmental models

- **Susceptible (S):** An individual has never had the disease and is susceptible to being infected;
- **Infected (I):** An individual who currently has the disease and can infect other individuals, and
- **Resistant/Recovered (R):** An individual does not have the disease, cannot infect others, and cannot be infected (sometimes called removed)

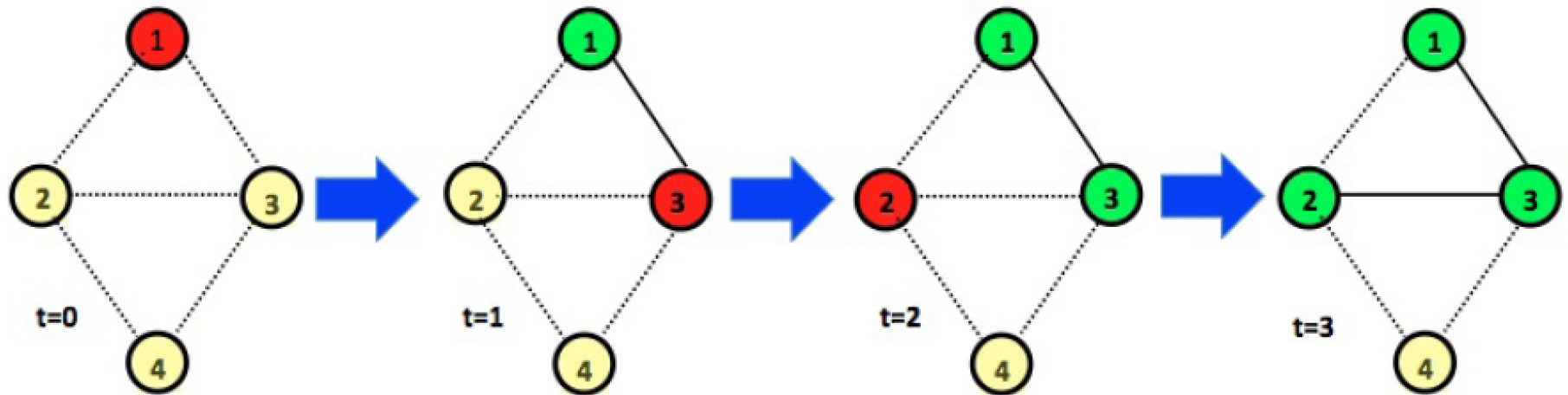


$$\begin{aligned}\frac{ds}{dt} &= -\beta is \\ \frac{di}{dt} &= \beta is - \gamma i \\ \frac{dr}{dt} &= \gamma i\end{aligned}$$





# Networked epidemiology

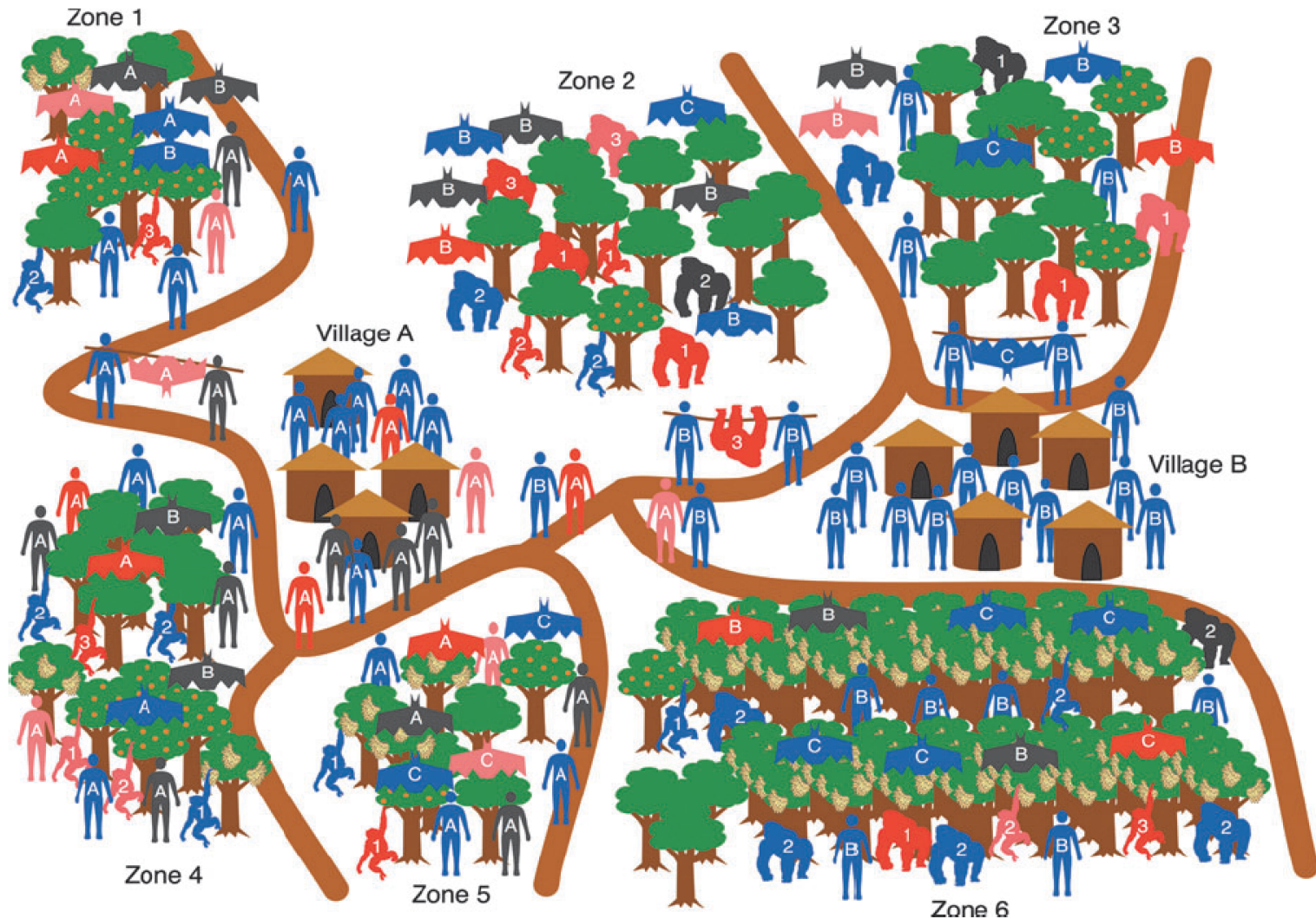


Fixed point:  $R = \{1, 2, 3\}$  and  $S = \{4\}$   
 $p(1, 3)(1 - p(1, 2))p(2, 3)(1 - p(2, 4))(1 - p(3, 4))$

- Each node is in states S (susceptible), I (infectious) or R (recovered)
- Time is discrete
- Each infected node  $u$  spreads the infection independently to each susceptible neighbor  $v$  with probability  $p(u, v)$
- Infected node  $u$  recovers after 1 time step
- *Fixed point*: all nodes in states S or R



# A Multi-scale modeling approach: networked epidemiology and agent-based models



**FIG. 7.** In an agent-based approach, individual behaviors and interactions can be represented across multiple coupled networks. These interactions can induce changes in the entities, which can, in turn, change which entities they interact with, and the nature of the interactions themselves.





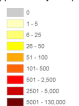
# Workflow for synthetic networks and populations

Data at URL: <https://www.vbi.vt.edu/ndssl/featured-projects/ebola>

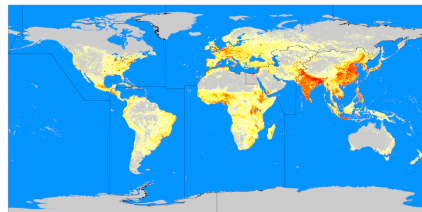
## LandScan Population Counts

Current Population Distribution\*

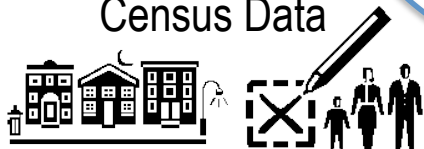
Number of Persons per 30 arc-second (approximately 1 km):



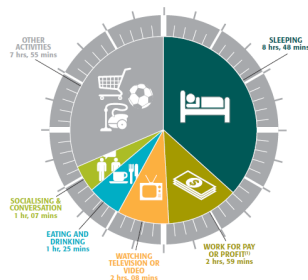
\*Population data are from Global Landscan 2007 prepared by the Oak Ridge National Laboratory



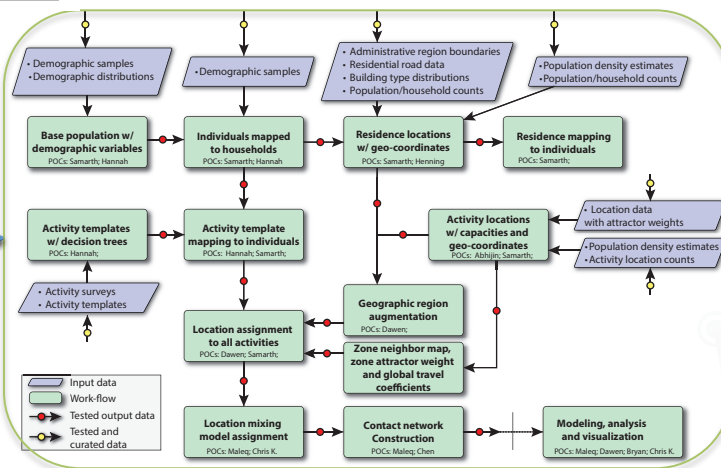
## Census Data



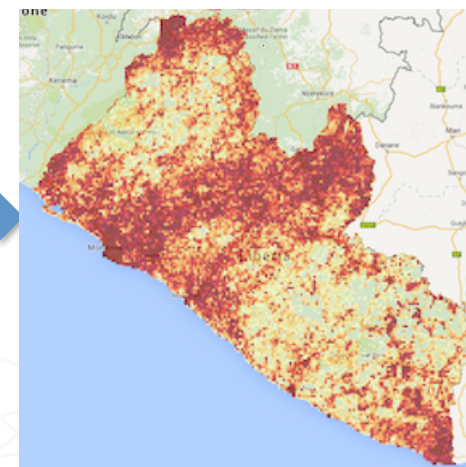
## Time Use Surveys



## Synthetic Population Pipeline



## Synthetic Population



- Automatic execution of workflows
- Integrated data testing
- Data quality measures
- Configuration Management



# ... Produces synthetic networks are dynamic & relational

*People*

*Locations*

Vertex attributes:

- age
- household size
- gender
- income
- ...



Vertex attributes:

- (x,y,z)
- land use
- ...

Edge attributes:

- activity type: shop, work, school
- (start time 1, end time 1)
- (start time 2, end time 2)
- ...

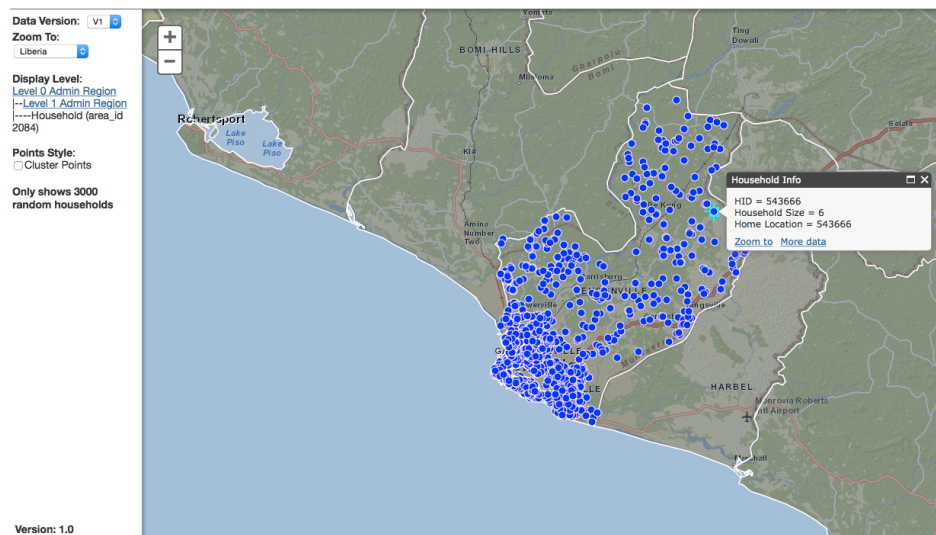
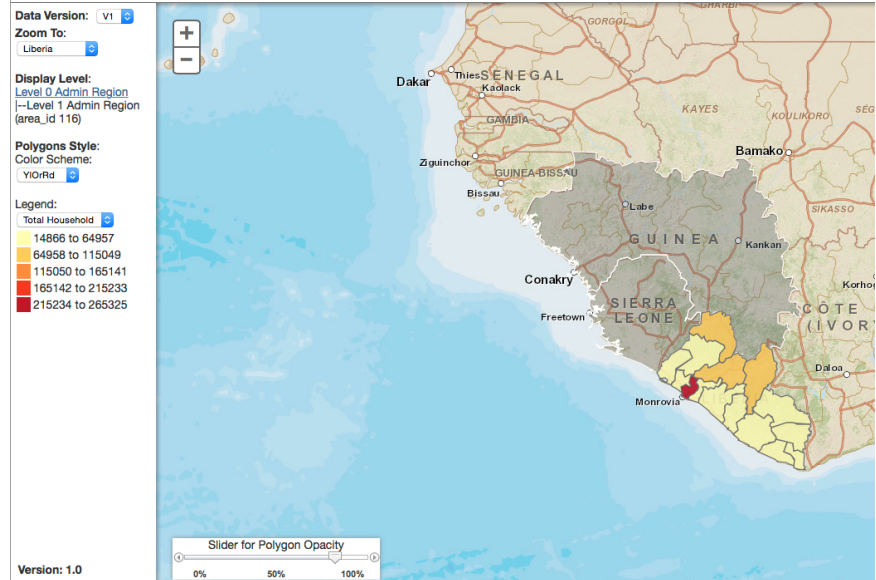


SIV: [ndssl.vbi.vt.edu/apps/siv](http://ndssl.vbi.vt.edu/apps/siv)

SIV: synthetic population visualization tool.

- Each synthetic individual is placed in a household with other individuals and household is located geographically
- Census of our synthetic population is statistically indistinguishable from the original census data.
- Multi-resolution: Explore individual or household level or county level, national attributes
- Users can visualize individual attributes and their interrelationships within a household
- Two versions - US and International

Synthetic Information Viewer (for Ebola Countries)





# Synthetic West Africa: Demographics

Country	ID	$ P $	$n_{HH}$	$n_H$	$n_W$	$n_S$	$n_C$	$n_A$
Sierra Leone	SLE-v1	5,743,725	989,917	989,917	134,847	9,617	5	23,663,983
Guinea	GIN-v1	11,521,656	2,375,532	2,375,532	250,096	9,317	6	55,069,905
Liberia	LBR-v1	4,092,310	844,066	844,066	88,016	5,477	20	22,202,262
Liberia	LBR-2gp	4,092,310	844,066	844,066	85,395	5,498	25	22,502,300
Liberia	LBR-9gp	4,092,310	844,066	844,066	85,395	5,498	25	20,144,766
Liberia	LBR-ldt	4,092,310	844,066	844,066	88,016	5,477	20	22,202,262

Quantity	Meaning
ID	population identifier
$ P $	population size
$n_{HH}$	number of household units
$n_H$	number of residence locations
$n_W$	number of work locations
$n_S$	number of school locations
$n_C$	number of colleges
$n_A$	total number of activities per day

Measure	Synopsis
$ P $	size of population
$ V $	number of vertices
$ E $	number of edges
$d_{\min}$	minimal degree
$d_{\max}$	maximal degree
$\bar{D}$	average degree
$\lambda_1$	largest eigenvalue of adjacency matrix
$\lambda_2$	second largest eigenvalue of adjacency matrix
$n_C$	number of components
$ V_{\max} $	size of largest components
$r$	relative size of largest component $ V_{\max} / V $
$D$	diameter
$n_T$	number of labeled (?) triangles
$\bar{c}$	average cluster coefficient





# West Africa: Social contact network properties

Population	$ P $	$ V $	$ E $	$d_{\min}$	$d_{\max}$	$d$	$\lambda_1$	$\lambda_2$
GIN-v1	11,521,656	11,425,439	183,268,217	0	255	32.69	124.84	124.70
SLE-v1	5,743,725	5,733,911	93,734,286	0	164	32.69	97.84	97.81
LBR-v1	4,092,310	4,084,569	84,789,847	0	249	41.52	125.48	125.34
LBR-2gp	4,092,310	4,077,272	87,255,911	0	254	42.80	126.83	126.41
LBR-9gp	4,092,310	4,077,426	78,830,017	0	250	38.67	111.97	111.93
LBR-ldt	4,092,310	4,079,500	146,386,825	0	721	71.77	202.99	195.47

Population	$n_C$	$ V_{\max} $	$r$	$D$	$n_T$	$\bar{c}$
GIN-v1	115,224	11,113,955	0.973	21	1,457,330,472	0.67
SLE-v1	10,543	5,704,544	0.995	16	683,523,753	0.61
LBR-v1	14,073	4,051,099	0.992	18	720,629,723	0.59
LBR-2gp	10,106	4,053,906	0.994	16	824,000,000	0.59
LBR-9gp	10,014	4,054,303	0.994	17	679,000,000	0.59
LBR-ldt	3,611	4,071,515	0.998	11	1.52841e+09	0.47





# High performance computing simulations

Distinguishing Features	EpiSimdemics (SC'09,WSC'10, IPDPS'14)	EpiFast (ICS'09)	Indemics (ICS'10,TOMACS'11)
<i>Solution Method</i>	Interaction-Based Simulation	Combinatorial +discrete time	Interaction-based, Interactive Simulations
<b><i>Performance 180 days 9M hosts &amp; 40 proc.</i></b>	<b>1 min (300K cores) for 300Million nodes</b>	<b>~40 seconds</b>	<b>15min-1hour</b>
<i>How was the method used</i>	Modeling detailed interactions at hospitals and funerals	Calibration and forecasting	Contact tracing based detection and interventions
<i>Disease transmission model</i>	Edge as well as vertex based (e.g. threshold functions)	Edge based, independence of infecting events	Edge based
<i>Query and Interventions</i>	Scripted, groups allowed but not dynamic	Scripted and specific groups allowed	Very general: no restriction on groups



# SIBEL: <http://sibeldemo.vbi.vt.edu/sibel/sibel.html>

- Web based tool for in-silico epidemiological experiments based on realistic social network simulations.
- Interactive, easy to use GUI
- Specifies factorial designs to investigate range of parameters
- Useful for planning and course of action of analysis activities for analysts.

SIBEL | VIRGINIA BIOINFORMATICS INSTITUTE  
AT VIRGINIA TECH

Welcome Sample User | Feedback | Logout

EXPERIMENTS ANALYSIS INITIAL CONDITIONS DISEASE MODELS TRIGGERS REGIMENS ADMIN ABOUT

### Experiments

My All Archived

Experiment ID	Status	Cells	Time	Sample	Actions
[2643] Ebola Analysis_Liberia	Running	3 Cells	Nov 20 2014, 01:51	Sample	START More Actions
[2683] SpatialSpreadLiberia...	Complete	1 Cell	Nov 20 2014, 01:30	Sample	START More Actions
[2682] Liberia - Travel - EVD...	Complete	1 Cell	Nov 19 2014, 23:38	Sample	START More Actions
[2676] Liberia - Travel - EVD...	Complete	3 Cells	Nov 18 2014, 08:30	Sample	START More Actions
[2663] Ebola Analysis_Liber...	Complete	3 Cells	Nov 17 2014, 14:21	Sample	START More Actions
[2652] Ebola Analysis_Liber...	Complete	3 Cells	Nov 15 2014, 12:36	Sample	START More Actions
[2609] Liberia	New	3 Cells	Nov 12 2014, 09:18	Sample	START More Actions
[2480] Liberia -1 with intev...	Complete	1 Cell	Oct 31 2014, 10:03	Sample	START More Actions

1 2 3

### Ebola Analysis\_Liberia

#### Details

Replicates	25
Total Cells	3
Simulated Days	200
Model	EpiFast

#### Region

Content may n...

#### Disease Models

AL\_25 Strong flu

##### Incubation Period

Probability Day 0 1 2 3

##### Infectious Period

Probability Day 0 1 2 3 4 5 6

#### Initial Conditions

5\_FIRST\_DAY

OnDay0

5

#### Enabled Interventions

Vaccine (1)



# Supporting real-time response using pervasive web-apps, multi-scale models and synthetic populations/networks



# Ebola Research Activities

- Situational Awareness
  - Situation reports / Facebook
  - Twitter
- Deterministic Compartmental Model
  - Simple forecasting and many experiments
- Stochastic Compartmental Model
  - Intervention effectiveness, forecasting with stochastic variation
- Network and population synthesis
- Agent-based Simulations
  - US likelihood experiments
  - Adaption of modeling framework to Ebola-like disease transmission and intervention
  - National spread models in West Africa
  - Evaluation of stochasticity
  - Calibration of detailed models
  - Vaccine stockpile experiments



# Support for Ebola Related Requests

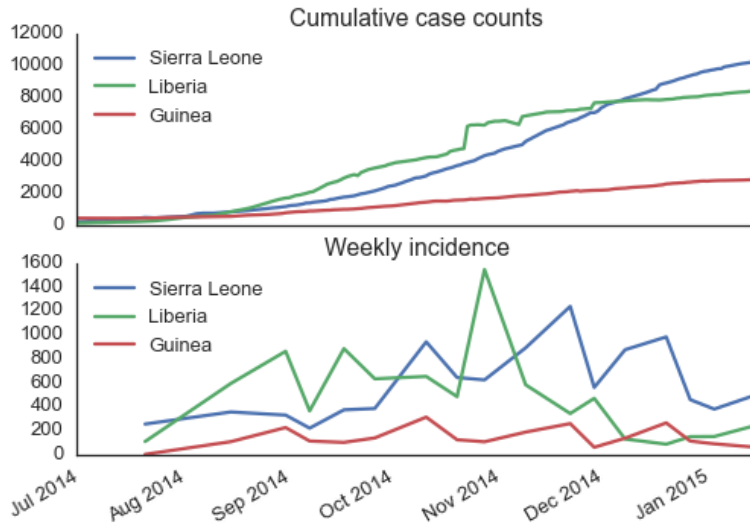
Supported 4 official requests

- **SOUTHCOM**
  - Risk assessment of disease spread risk with cases imported to Central and South American nations
- **NORTHCOM**
  - Risk assessment of disease spread risk with cases imported to Mexico and Caribbean nations
- **Regional Contingency Team – Ebola (RCT-E)**
  - Risk assessment of disease spread risk with cases imported to surrounding West African nations
- **NORTHCOM: Amalgam Dragon**
  - Training exercise using hypothetical Ebola as bioterror weapon in US population (prior to West African crisis)





# Maintaining Situational Awareness



- Keep decision-makers appraised of the situation
  - Up to October, no larger organizations provided such analyses
- Required integration, organization, analysis, and interpretation of multiple sources of information
- Use this understanding to design simulation experiments



# Maintaining Situational Awareness

## Ebola Case and Death Summary by County

County	DAILY EMAIL REPORT New <sup>1</sup> suspected and probable cases (Alive and Dead)			Laboratory <sup>2</sup> Confirmed Cases (Alive and Dead)	Confirmed Cases on Contact List	Cumulative <sup>3</sup> cases 23 May- FEBRUARY 9th 2015				Cumulative deaths <sup>2</sup>
	Total	Suspect	Probable			Total	Suspect	Probable	Confirmed	
Bomi	1	1	0	0	0	319	101	79	139	174
Bong	3	3	0	0	0	601	417	38	150	159
Gbarpolu	0	0	0	0	0	35	16	3	16	13
Grand Bassa	0	0	0	0	0	182	55	73	54	80
Grand Cape Mount	0	0	0	0	0	320	178	52	94	201
Grand Gedeh	0	0	0	0	0	11	8	0	3	6
Grand Kru	0	0	0	0	0	36	14	18	4	27
Lofa	1	1	0	0	0	679	195	146	332	405
Margibi	0	0	0	0	0	1292	460	441	391	582
Maryland	2	2	0	0	0	28	22	2	4	23
Montserratado	31	31	0	0	0	4932	2290	871	1794	2059
Nimba	0	0	0	0	0	337	90	131	116	60
River Gee	3	3	0	0	0	28	16	5	8	16
River Cess	0	0	0	0	0	44	10	10	24	27
Sinoe	0	0	0	0	0	61	36	7	18	26
NATIONAL	41	41	0	0	0	8864	3876	1869	3147	3846

<sup>1</sup> From daily email county reports of aggregated data for that day

<sup>2</sup> Laboratory confirmed cases of suspects and probable cases identified during the preceding days

<sup>3</sup> From individual-level data from the Case Investigation form; cases may be reclassified according to surveillance case definitions ↑ Increase in daily reported cases by county ■ County did not report

cmrivers / ebola

Watch 43 Star 211 Fork 148

branch: master ebola / liberia\_data / 2014-09-26-v134.csv

jsoma on Oct 16, 2014 rename River Cess County to RiverCess County

2 contributors

33 lines (32 sloo) 2.607 kb

Raw Blame History

	Date	Variable	National	Bomi County	Bong County	Gbarpolu County	Grand Bassa	Gr
1								
2	09/26/2014	Specimens collected						
3	09/26/2014	Specimens pending for testing						
4	09/26/2014	Total specimens tested						
5	09/26/2014	Newly reported deaths	64	2	4	0	0	0
6	09/26/2014	Total death/s in confirmed cases	882	29	14	0	17	6
7	09/26/2014	Total death/s in probable cases	656	33	21	0	9	3
8	09/26/2014	Total death/s in suspected cases	437	4	70	0	7	5
9	09/26/2014	Total death/s in confirmed, probable, suspected cases	1975	66	105	0	33	14
10	09/26/2014	Case Fatality Rate (CFR) - Confirmed & Probable Cases						
11	09/26/2014	Newly reported contacts	283	0	10	0	0	0
12	09/26/2014	Total contacts listed	12921	549	767	0	263	80
13	09/26/2014	Currently under follow-up	6774	441	170	0	161	77
14	09/26/2014	Contacts seen	6425	440	170	0	161	0
15	09/26/2014	Contacts who completed 21 day follow-up	287	101	0	0	0	0
16	09/26/2014	Contacts lost to follow-up	19	2	0	0	0	0
17	09/26/2014	New admissions	31	0	5	0	0	0

<https://github.com/cmrivers/ebola>

Situation reports, Facebook updates, WHO reports, etc. were digitized (often from PDF tables) into a more computable CSV format shared via GitHub.



# Maintaining Situational Awareness

Most common images:



Prénoms	
Garçon	Fille
Noel	Noëlla
Emmanuel	Emmanuela
Daniel	Daniella
Ebo	??????????

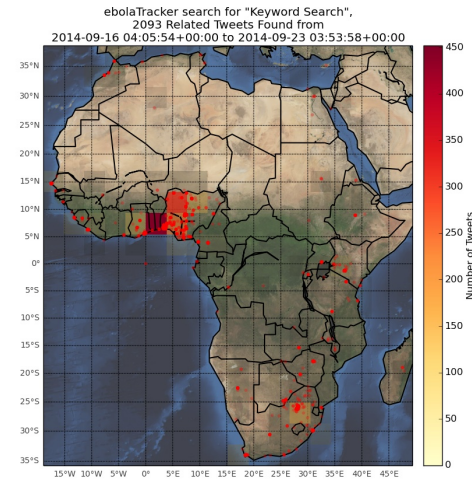
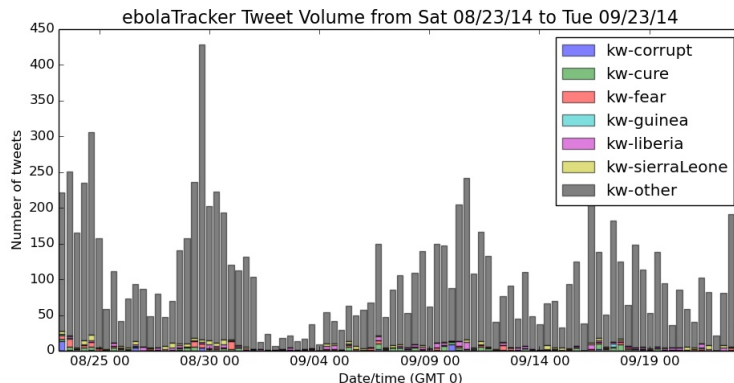


Photo content: Solidarity with Ebola affected countries, Jokes about bushmeat, Ebola risk, names, positive health message

Twitter Scraping began in mid-August, Of any mention of Ebola in Africa. This tool also extracts images from tweets and keeps track of the most popular ones as depicted here (Week of Sept 17-23). The most common tweets this week were about fighting Ebola, and a few jokes indicating a grown fear and awareness of the threat posed by Ebola.





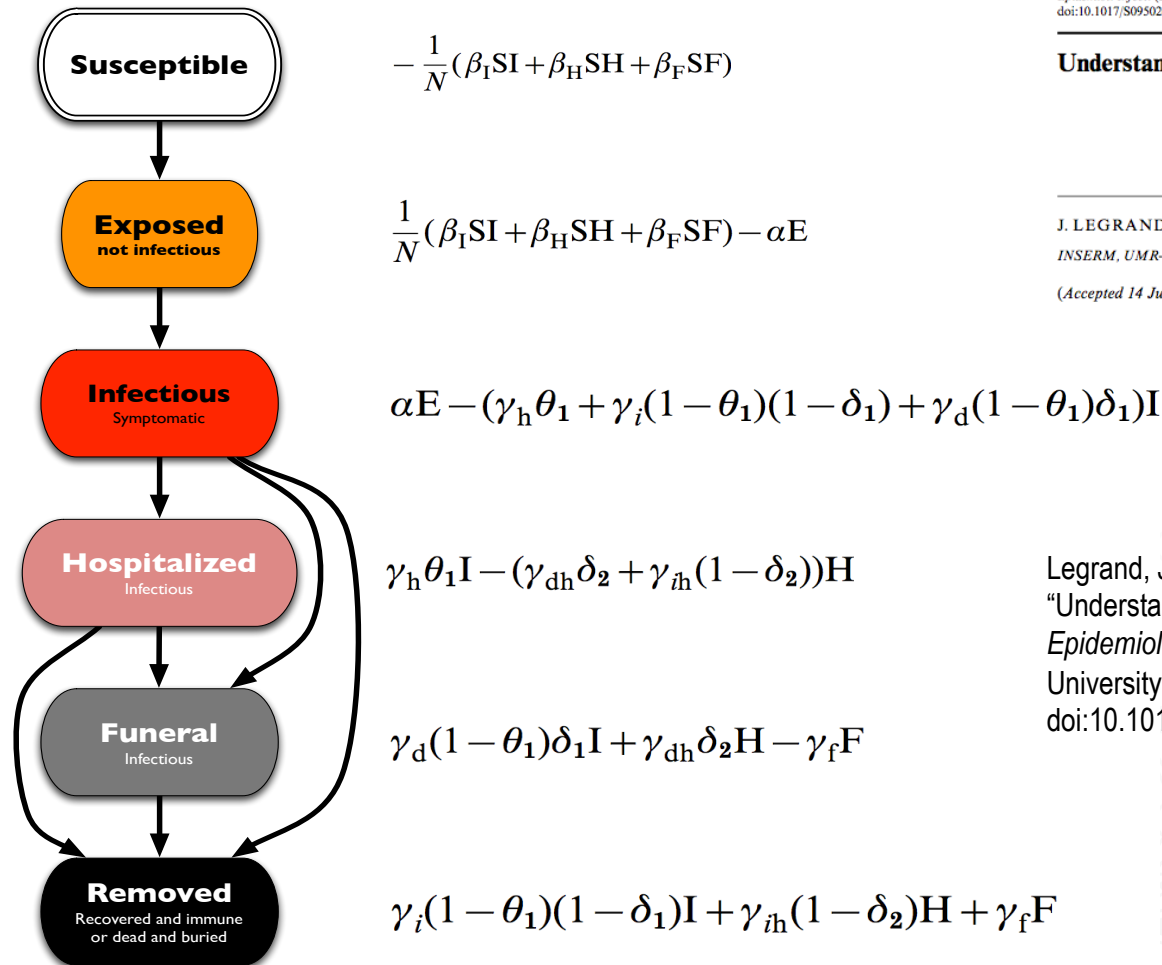
# Modeling Ebola: Compartmental model

*Epidemiol. Infect.* (2007), 135, 610–621. © 2006 Cambridge University Press  
doi:10.1017/S0950268806007217 Printed in the United Kingdom

## Understanding the dynamics of Ebola epidemics

J. LEGRAND\*, R. F. GRAIS, P. Y. BOELLE, A. J. VALLERON AND A. FLAHAULT  
*INSERM, UMR-S 707, Paris, France, and Université Pierre et Marie Curie-Paris 6, UMR-S 707, Paris, France*  
(Accepted 14 July 2006; first published online 26 September 2006)

Legrand, J, R F Grais, P Y Boelle, A J Valleron, and A Flahault.  
“Understanding the Dynamics of Ebola Epidemics”  
*Epidemiology and Infection* 135 (4). 2007. Cambridge  
University Press: 610–21.  
doi:10.1017/S0950268806007217.

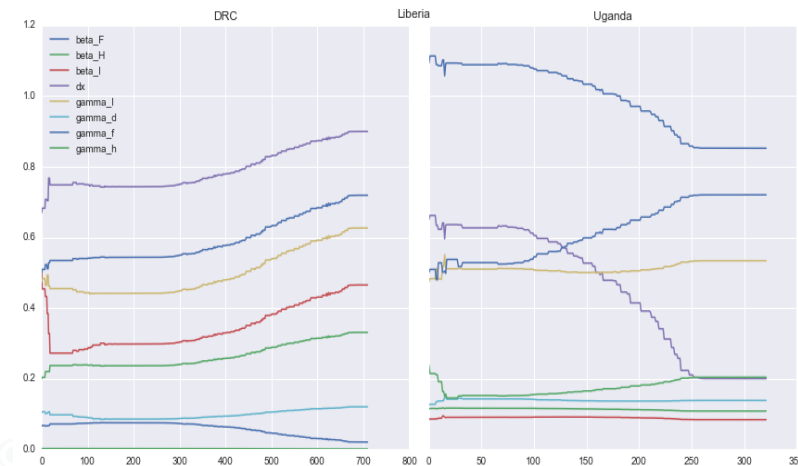






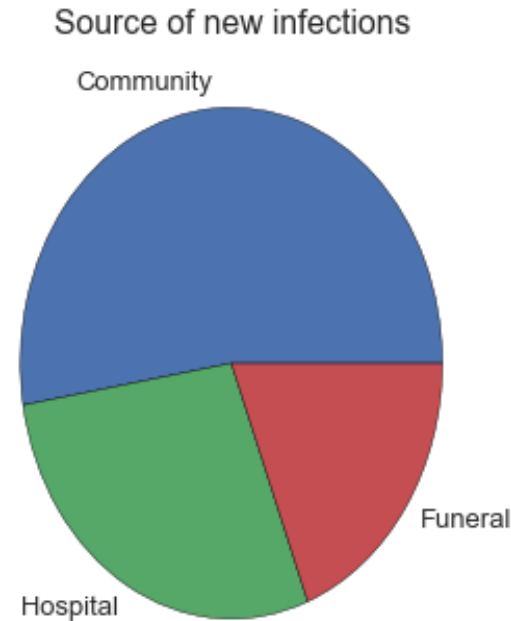
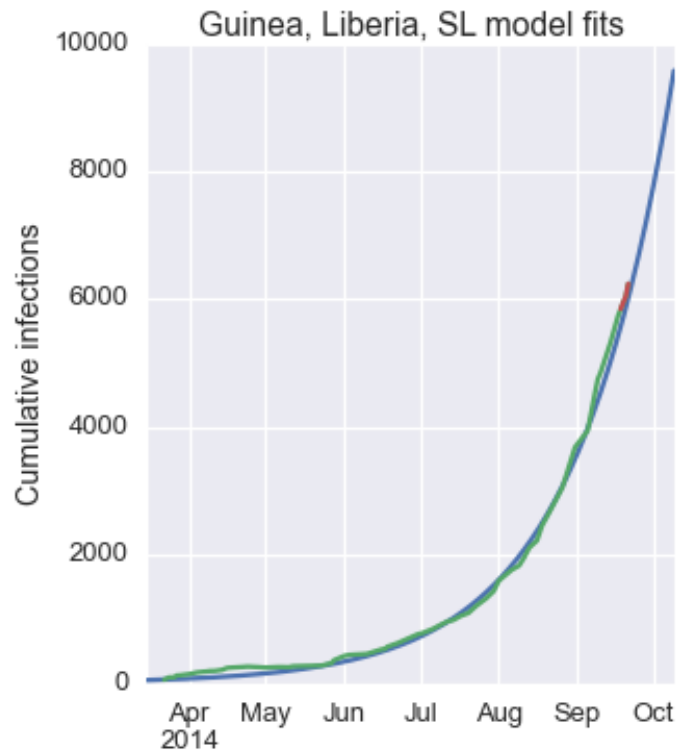
# Modeling Ebola: Optimized Fit Process

- Parameters to explored selected
  - Diag\_rate, beta\_I, beta\_H, beta\_F, gamma\_I, gamma\_D, gamma\_F, gamma\_H
  - Initial values based on two historical outbreak
- Optimization routine
  - Runs model with various permutations of parameters
  - Output compared to observed case count
  - Algorithm chooses combinations that minimize the difference between observed case counts and model outputs, selects “best” one





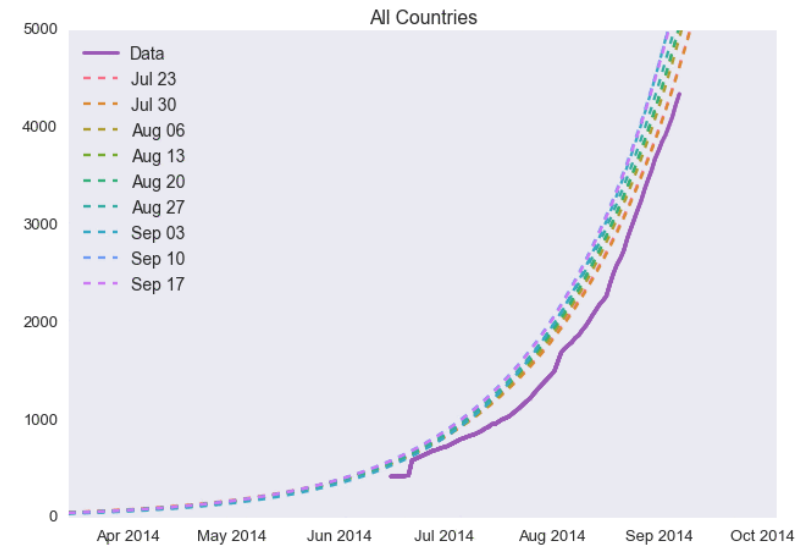
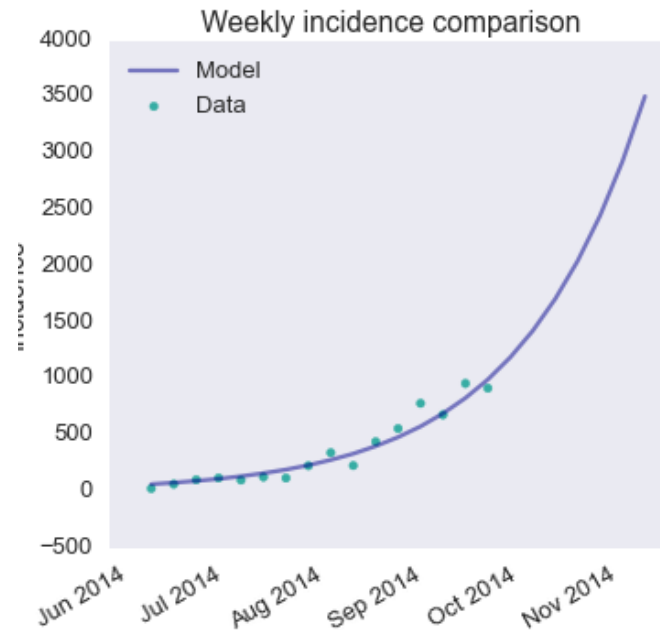
# Ebola Model: Estimates



rl: 1.1  
rH:0.4  
rF:0.3  
**Overall:1.7**



# Ebola Model: Estimates



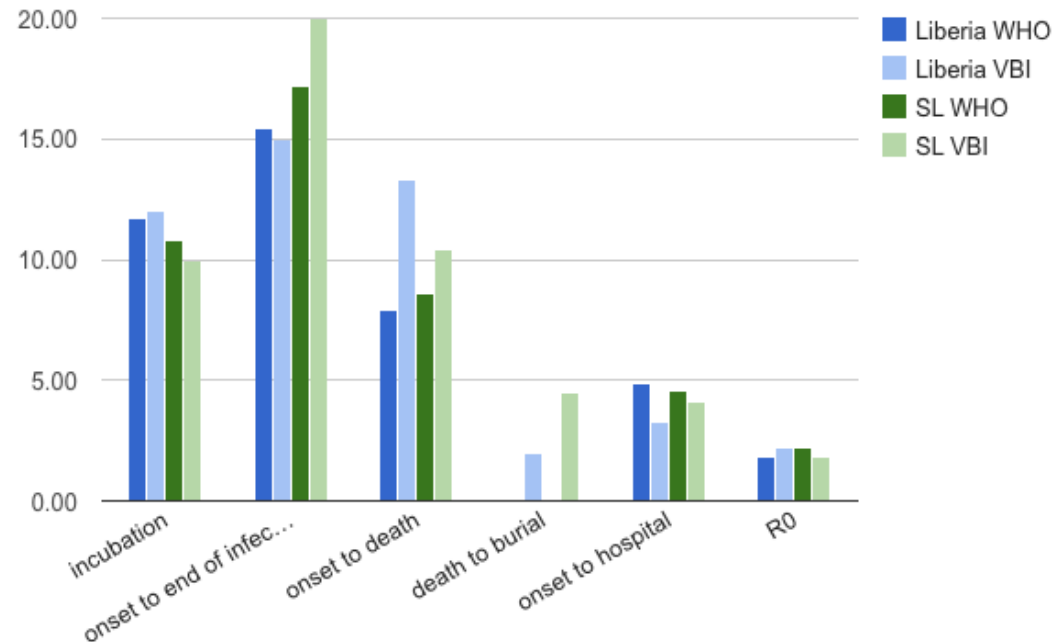
	8/10 – 8/16	8/17 – 8/23	8/24 – 8/30	8/31 – 9/6	9/8 – 9/13	9/14 – 9/20	9/21 – 9/27	9/28 – 10/4
Actual	231	442	559	783	681	959	--	--
Forecast	336	403	483	578	693	830	994	1191



# Ebola Model: Evaluation

- Late September WHO published results from the detailed epidemiologic data
- Estimates derived from the fitted compartmental model were very close to that measured by the WHO.

Interval comparison



parameter	name	Liberia WHO	Liberia VBI	SL WHO	SL VBI	Vespignani	Althaus	Towers	Nishiura	Fisman	Meltzer
alpha	incubation	11.70	12.00	10.80	10.00	7.0	5.3	5, 7, 10			6
gamma_i	onset to end of infectiousness for survivors	15.4	15.0	17.2	20.0	10.0	5.6 (infectious period)	5, 7, 10 (infectious periods)			6 (infectious period)
gamma_d	onset to death	7.9	13.3	8.6	10.4	9.6					
gamma_f	death to burial		2.0		4.5	2.0					
gamma_h	onset to hospital	4.9	3.2	4.6	4.1	5.0					
What exactly they claim to be measuring varies	R0	1.8	2.2	2.2	1.8	1.8 overall	SL 2.5 & 1.6 Liberia, but has time-decaying beta that puts R < 1 in early July	1.3 SL & 2.1 Liberia	1.4-1-7 overall	8.3 SL & 1.7 Liberia	





# Eyes-on-the-Ground

Describe the road conditions between two regions in Sierra Leone

**Origin:** Binkolo (Bombali)

**Destination:** Kamabai (Bombali)

**Date of Observation:** 02/18/2015  
Last reported: 01/27/2015  
Total Responses: 1 [See Results](#)

**Road condition:**  
Last reported: unknown

**Travel Duration:**  
enter time in mins  
Last reported: 36 minutes  
Mean: 36 minutes

**Traffic Level:**  
Last reported: unknown

**Any additional comments:**  
This field is optional

[submit new report](#) [change country](#)

So far a total of 5 reports on road conditions have been submitted to Eyes-on-the-Ground for this trip:

Date of Observation	Road Condition	Travel Duration	Traffic Level	Additional Comments
2012-01-13	unknown	36	unknown	initial report
2012-03-18	moderate	40	medium	

Below you see a history of other reports for this trip:  
Thank you for submitting the report on road conditions between **Binkolo (Bombali)** and **Kamabai (Bombali)**!

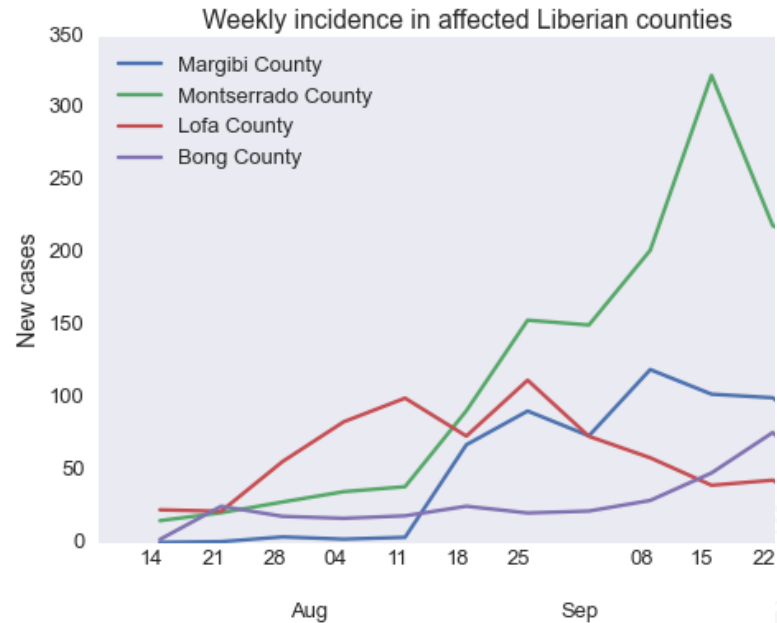
Eyes-On-The-Ground (Sierra Leone)

Provides easy to use, light weight interface to access and submit “on the ground” data to support analyses and simulations.



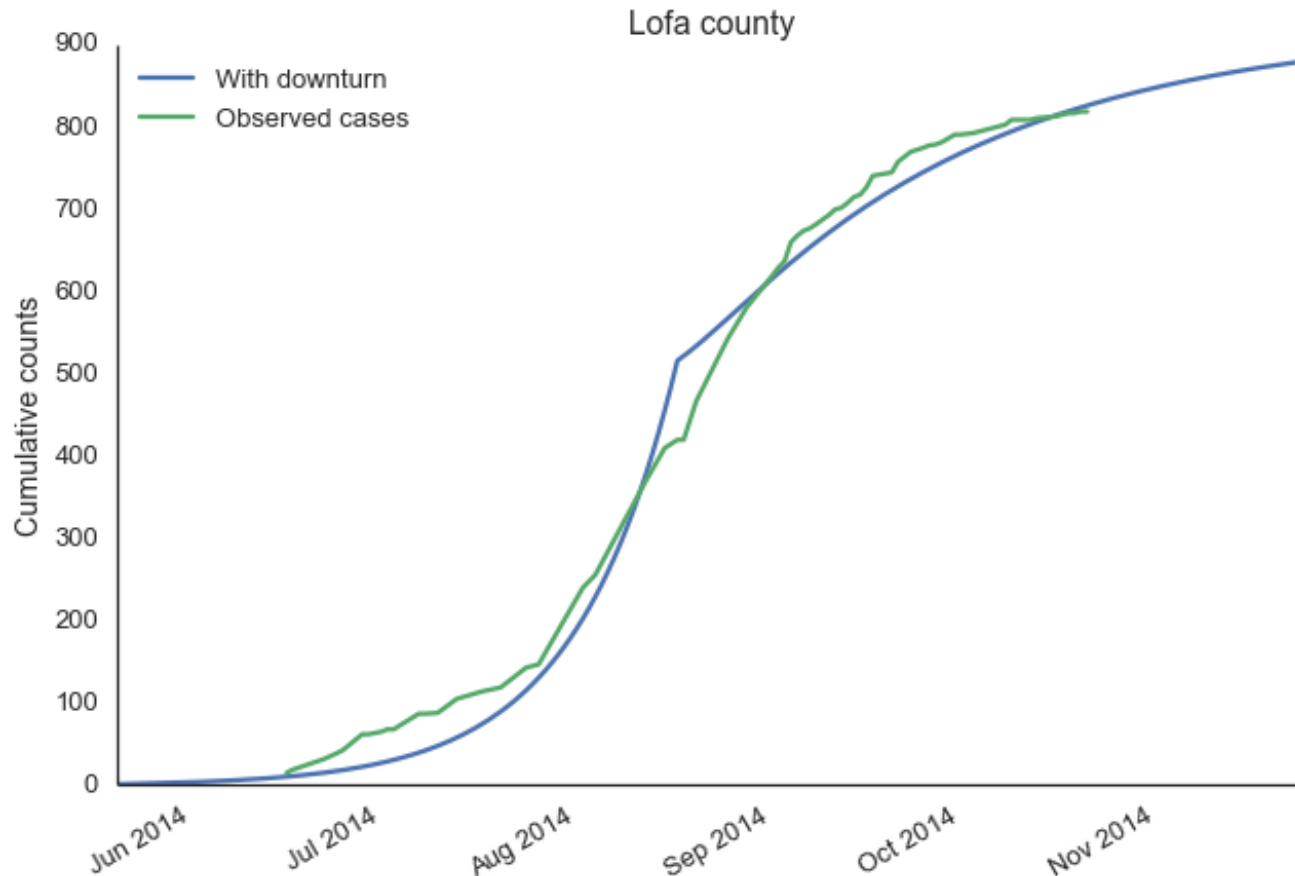
# Learning from Lofa

- Lofa county, near the epicenter of the Ebola outbreak
- Grassroots efforts and very active health director educated public and reducing transmission in community
- Experiment: What if the experience of Lofa county can be transferred to Liberia as a whole?





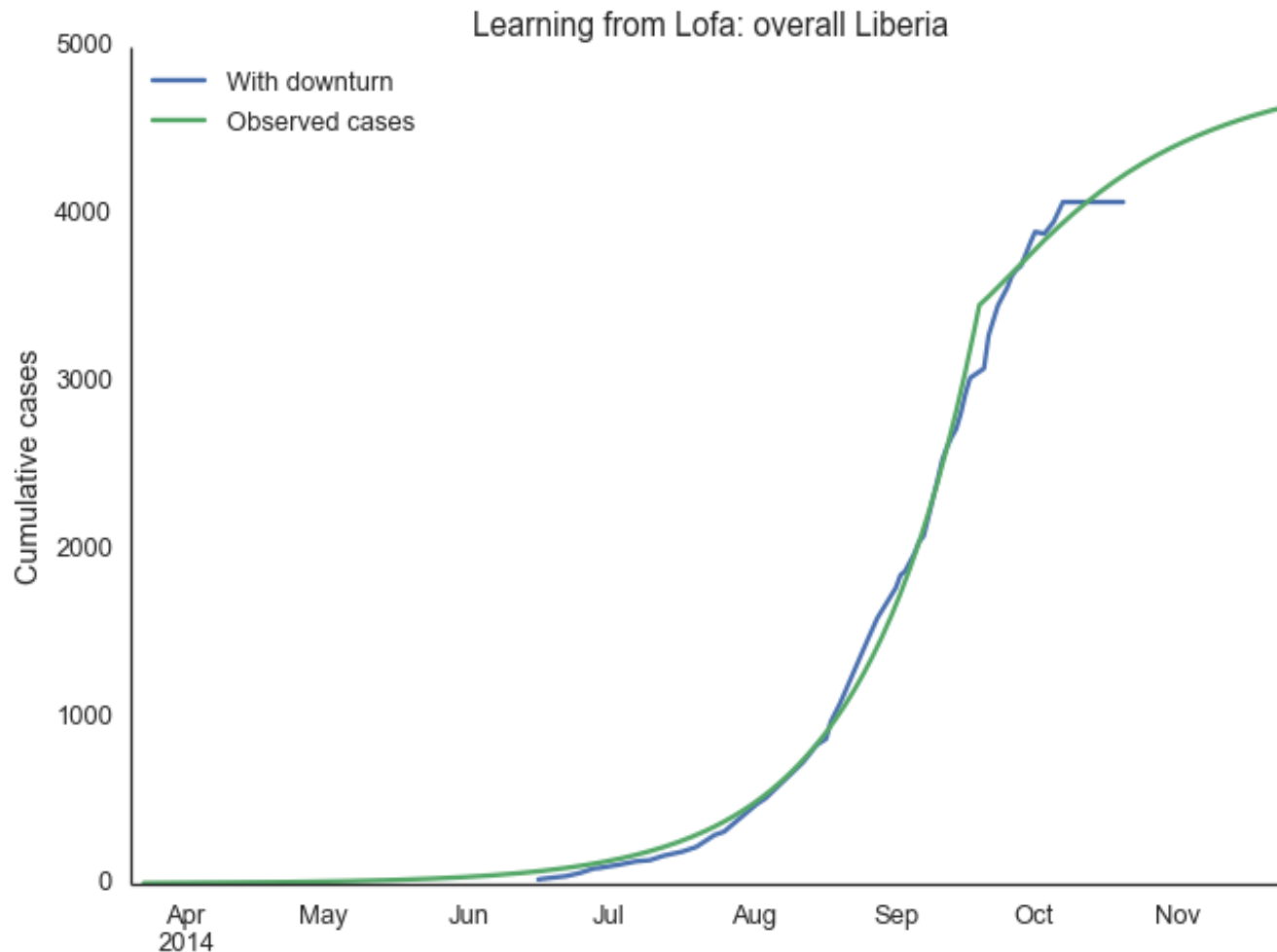
# Learning from Lofa



Model fit to Lofa case with a change in behaviors resulting in reduced transmission starting mid-Aug (blue), compared with observed data (green)



# Learning from Lofa

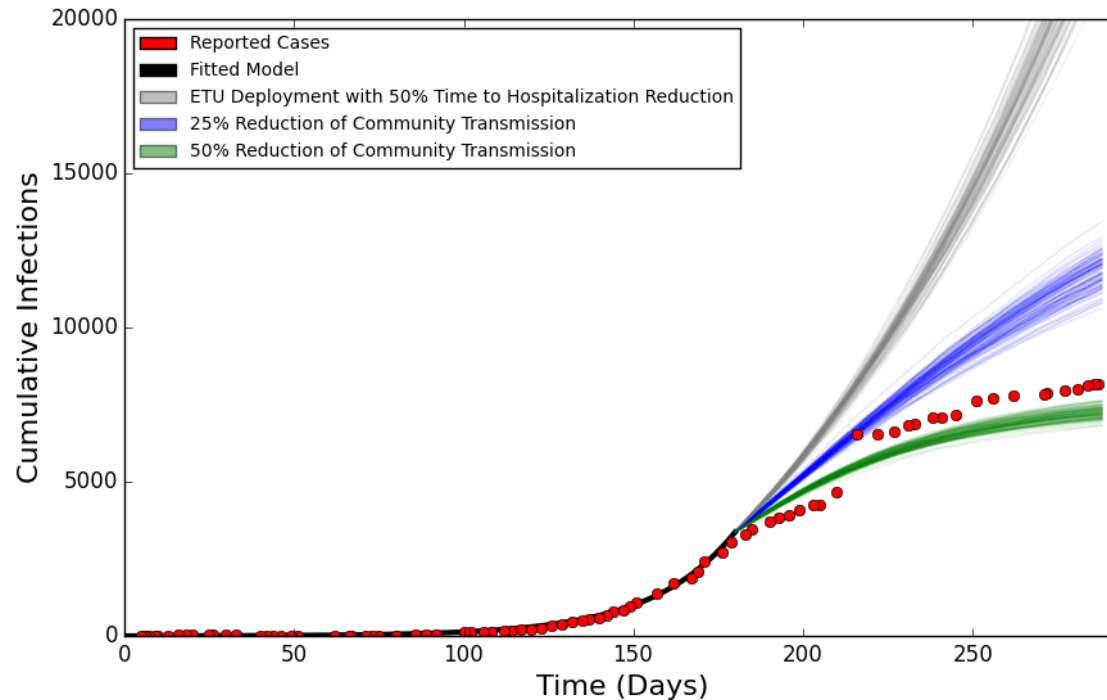


Model fit to Liberia case with a change in behaviors resulting in reduced transmission starting Sept 21<sup>st</sup> (green), compared with observed data (blue)





# Impact of ETUs



- How effective were the deployed Ebola Treatment Units?
- Significant reductions in community transmission required to match current observations



# Agent-based Modeling: Challenges

- Rapidly adapting system optimized for airborne transmission to support
  - novel disease model and transmission modes
  - Interventions and populations
- Parameterizing a data intensive model when data is scarce and often inaccurate
- Analysis of a disease process with high levels of variance and stochastic effects



# SIBEL Synthetic Information Based Epidemiological Laboratory

SIBEL | VIRGINIA BIOINFORMATICS INSTITUTE  
AT VIRGINIA TECH

Welcome Bryan Lewis | [Feedback](#) | [Logout](#)

**EXPERIMENTS** ANALYSIS INITIAL CONDITIONS DISEASE MODELS TRIGGERS REGIMENS ADMIN ABOUT

[Back](#) Liberia - EVD06 - calib 6.1 c... Total Cells 1 [View Cells](#)

**Enabled Interventions**

Summary **Generic Intervention** Vaccinate Social Distance Close Work Close School Pharmaceutical Treatment Pharmaceutical Prophylaxis Dynamic Sequestration

No enabled Generic Intervention [+ Create New](#)

Intervention Name:

**Subpopulation** ⓘ

Selection: All ⓘ

Type: All ⓘ

Category Total Change Percentage

All 100% (11521656) 100% (11521656)

**Trigger** ⓘ [New](#)

☐ On Day ☐ % Infectious

**Duration** ⓘ

☒ Value ☐ Sweep ⓘ

200 days

**Compliance** ⓘ

☒ % Value ☐ Sweep ⓘ

0%

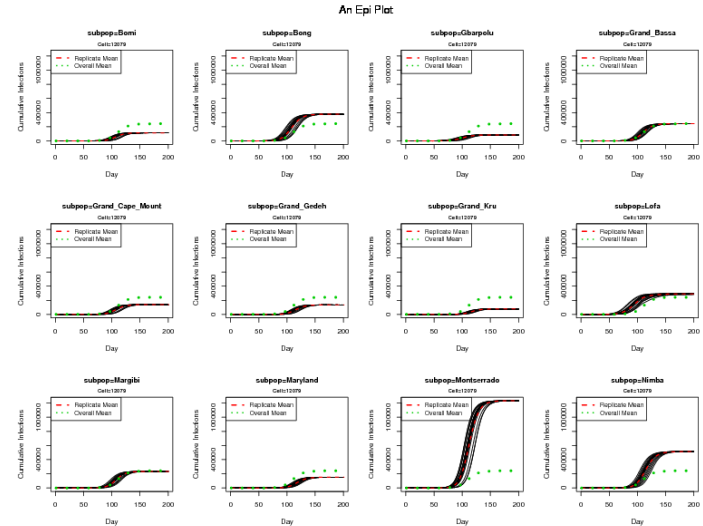
**Scaling Factor** ⓘ

	Home	Work	Shop	Other	School
Infectivity multiplier	1.0	1.0	1.0	1.0	1.0
Susceptibility multiplier	1.0	1.0	1.0	1.0	1.0

**Rate Of Administration** ⓘ

Rate Per Day  Unlimited ☒

[Delete](#) [Duplicate](#) [Cancel](#) [Save](#)



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Welcome Bryan Lewis | [Feedback](#) | [Logout](#)

**EXPERIMENTS** ANALYSIS INITIAL CONDITIONS DISEASE MODELS TRIGGERS REGIMENS ADMIN ABOUT

[Back](#) Liberia - Travel - EVD09 - Lo... Total Cells 1 [View Cells](#)

**Enabled Interventions**

Summary **Generic Intervention** Vaccinate Social Distance Close Work Close School Pharmaceutical Treatment Pharmaceutical Prophylaxis Dynamic Sequestration

**Your Interventions**

**Pharmaceutical Treatment**

[Funeral 80: All \(4092310\)](#)

[Hospital 80: All \(4092310\)](#)

**Generic Intervention**

[EbolaMode: All \(4092310\)](#)

Design, Execute, and Analyze  
Agent-based simulations of  
Infectious disease spread



# SIBEL extensions and refinements

---

- Flexible framework for modifications too complex to represent within web interface
- Contact based interventions prototyped
- Refinement of analysis tools
  - Enable interactive overview analyses
  - Tools to allow more flexible detailed analysis (eg custom-defined age groups, etc.)



# Agent-based Model in the US

- Early in the outbreak, concern about US spread was a primary question
- Existing US population data and simulation tools were harnessed to address this situation

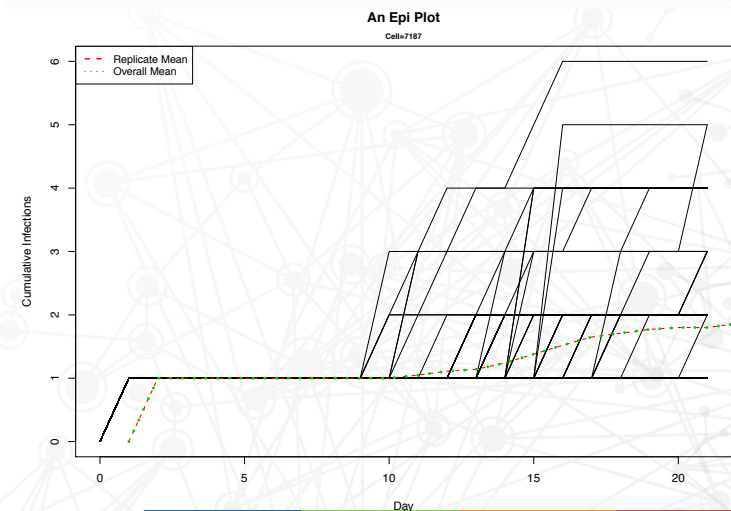
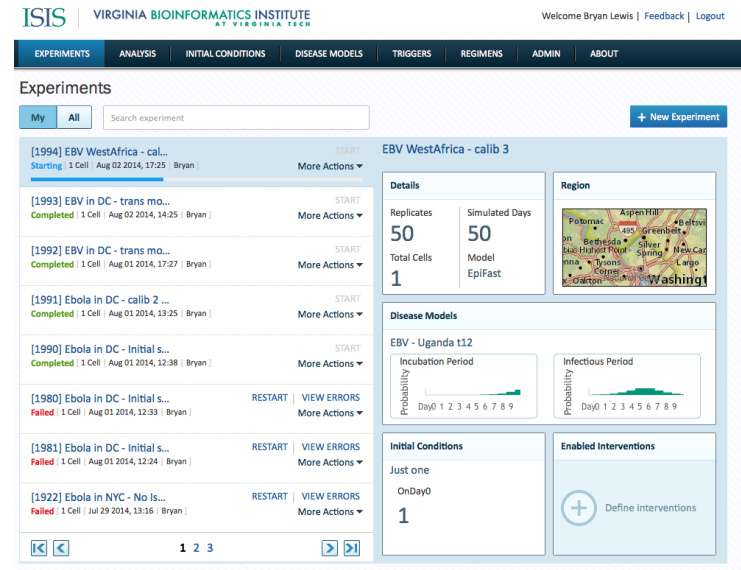
## Summary of results:

100 replicates

Mean of 0.8 additional cases

Max of 6 cases

Majority only one initial case

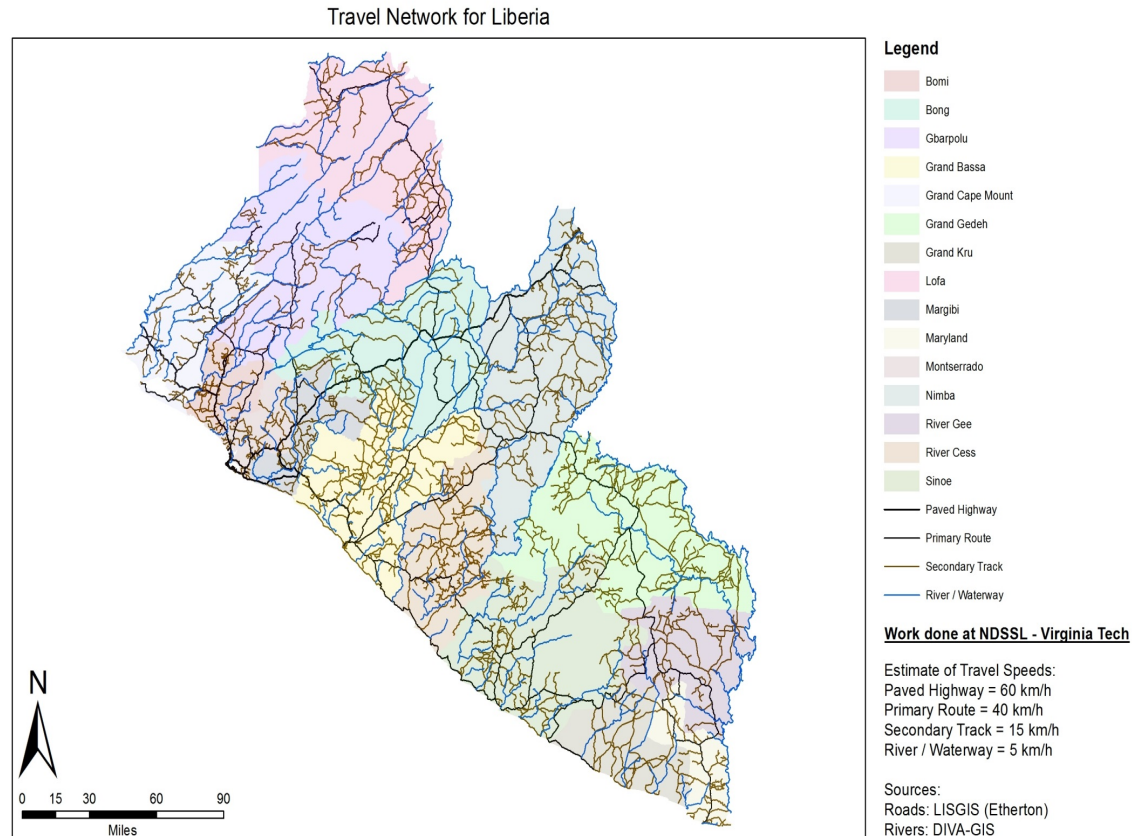






# National Spread

- Need to understand travel patterns
- Need to know transportation network





# National Spread



	Bomi	Bong	Gbarpolu	Grand Bassa	Grand Cape Mount	Grand Gedeh	Grand Kru	Lofa	Margibi	Maryland	Montserrado	Nimba	River Cess	River Gee	Sinoe
Bomi	0.36666666	0.55	0.5	1	0.5	0.425	0.425	0.1	1	0.425	1	0.55	0.1	0.425	0.3
Bong	0.55	0.3	0.3	0.55	0.3	1	1	1	1	1	1	1	0.1	1	7
Gbarpolu	0.5	0.3	0.3	0.5	0.5	0.425	0.425	0.1	0.5	0.425	0.5	0.3	0.1	0.425	0.3
Grand Bassa	1	0.55	0.5	0.5	0.5	0.3	0.3	0.4	1	0.3	1	0.55	0.1	0.3	0.3
Grand Cape Mount	0.5	0.3	0.5	0.5	0.5	0.3	0.3	0.5	0.3	0.5	0.5	3	0.1	0.3	0.3
Grand Gedeh	0.425	1	0.425	0.3	0.3	0.3	1	0.55	1	0.55	1	0.55	1	0.1	0.5
Grand Kru	0.425	1	0.425	0.3	0.3	1	0.55	0.53333333	1	0.53333333	1	0.1	1	0.5	0.5
Lofa	0.1	1	0.1	0.4	0.3	1	1	0.55	1	0.55	1	0.1	0.1	1	4
Margibi	1	1	0.5	1	0.5	0.55	3	0.55	3	0.53333333	1	1	0.1	3	0.3
Maryland	0.425	1	0.425	0.3	0.3	1	1	1	0.53333333	0.53333333	0.53333333	1	0.1	1	0.5
Montserrado	1	1	0.5	1	0.5	0.55	3	0.55	1	0.53333333	0.53333333	0.55	0.1	3	0.3
Nimba	0.55	1	0.3	0.55	0.23333333	1	1	1	1	1	1	0.55	0.1	0.1	0.23333333
River Cess	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1
River Gee	0.425	1	0.425	0.3	0.3	1	1	1	3	1	0.53333333	1	0.1	0.1	0.5
Sinoe	0.36666666	7	0.3	0.3	0.3	0.5	0.5	0.714	0.3	0.5	0.3	3	0.1	0.3	0.3

Green 1  
Red 0.5  
Black 0.3

Based on traveling from county capital to county capital  
Based on 17SEP2014 data

During the rainy season this road network is degraded, which influences the amount of travel. This in turn can drive where future cases occur and the overall size of the epidemic. More importantly its critical to understand when trying to decide where to devote resources to combat the epidemic.



Maryland Avenue from Pleebo to Harper (from John Etherton, Laboratory



# Eyes-on-the-Ground

Describe the road conditions between two regions in Sierra Leone

**Origin:**

**Destination:**

**Date of Observation:**  
  
Last reported: 01/27/2015  
Total Responses: 1 [See Results](#)

**Road condition:**  
  
Last reported: unknown

**Travel Duration:**  
  
Last reported: 36 minutes  
Mean: 36 minutes

**Traffic Level:**  
  
Last reported: unknown

**Any additional comments:**

Eyes-On-The-Ground (Sierra Leone)

Thank you for submitting the report on road conditions between **Binkolo (Bombali)** and **Kamabai (Bombali)**. Below you see a history of other reports for this trip.

Date of Observation	Road Conditions	Travel Duration	Traffic Level	Additional Comment
2015-02-18	passable	40	medium	
2015-01-27	unknown	36	unknown	Source: Telonis

So, far a total of **2** reports on road conditions have been submitted to Eyes-on-the-Ground for this trip.

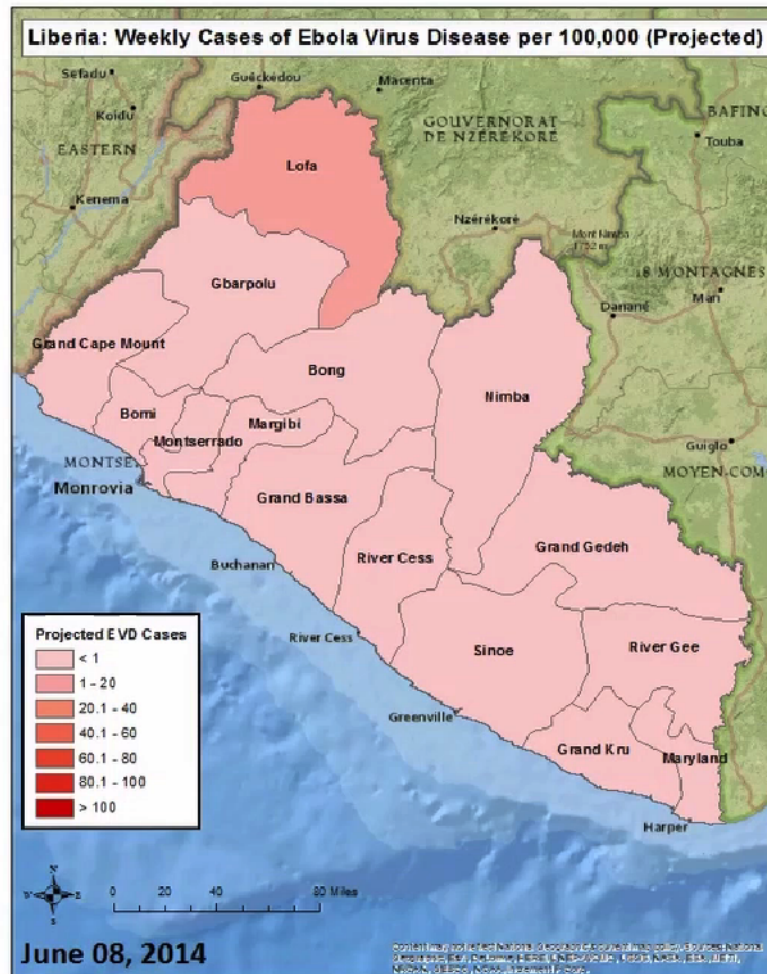
[Submit New Report](#) [Change Country](#)

Provides easy to use, light weight interface to access and submit “on the ground” data to support analyses and simulations.





# Ebola national model

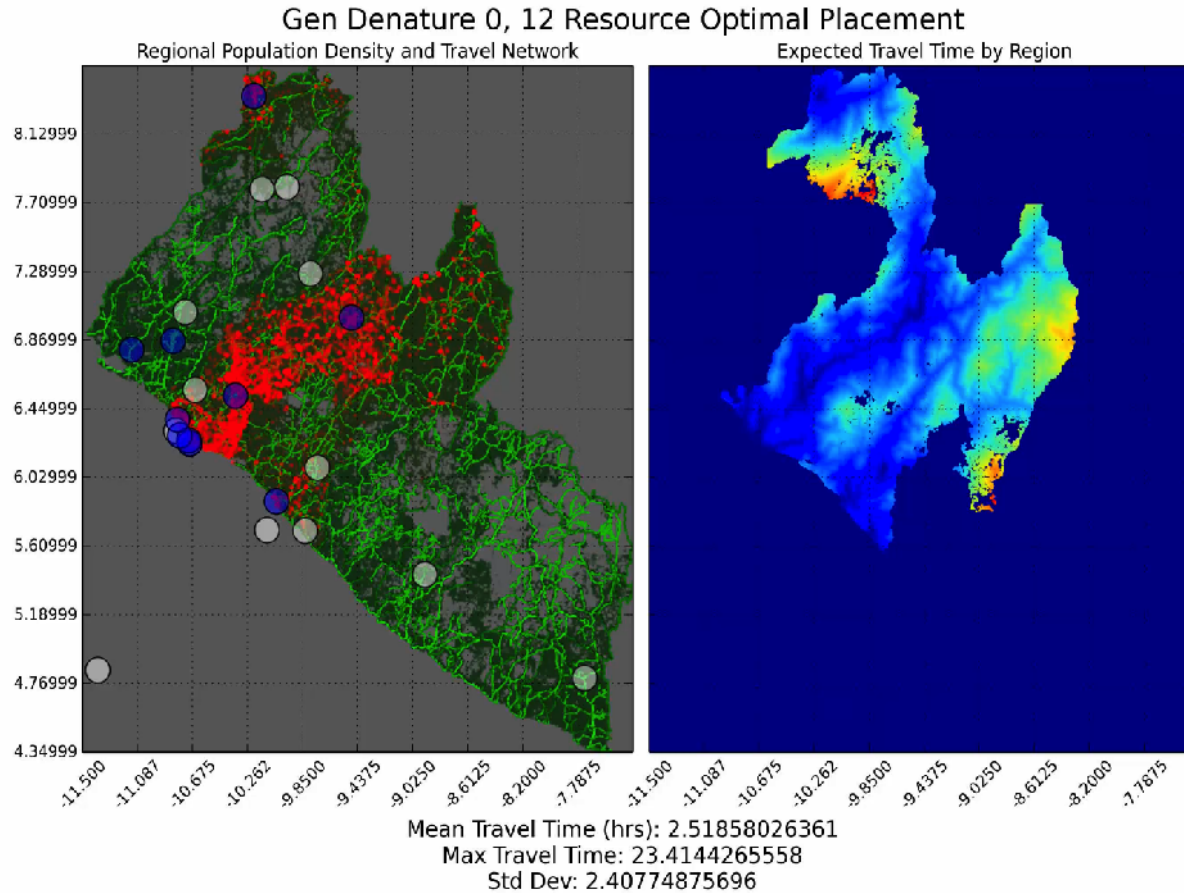


What  
counties  
will be  
affected  
next?





# Optimal Placement of ETUs

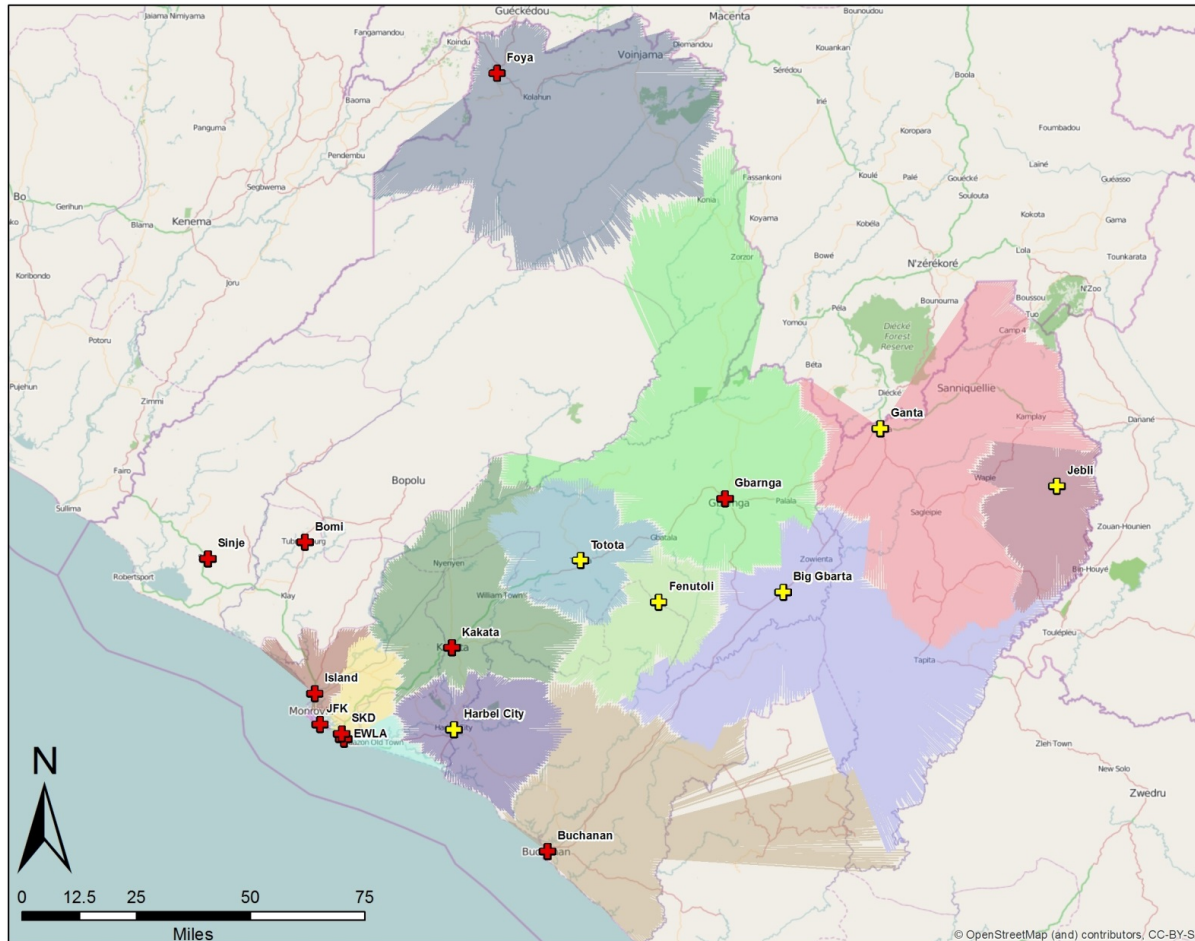






# Optimal Placement of ETUs

K-median Allocation of 6 new ETUs based on Predicted Ebola Cases on Dec-1st



ETUs	Cases	Long	Lat
All Monrovia	1,442	-10.7505	6.2411
Big Gbarta	246	-9.2951	6.7108
Bomi	1	-10.8207	6.8663
Buchanan	187	-10.0442	5.8834
Fenutoli	105	-9.6912	6.6790
Foya	187	-10.2130	8.3632
Ganta	237	-8.9851	7.2322
Gbarnga	598	-9.4812	7.0084
Harbel City	368	-10.3430	6.2709
Jebli	66	-8.4210	7.0482
Kakata	707	-10.3518	6.5313
Sinje	0	-11.1305	6.8129
Totota	290	-9.9418	6.8106

## Legend

- + Facility Already Built
- + Proposed Facility

Coordinate System: WGS 1984 UTM Zone 29N  
 Projection: Transverse Mercator  
 Datum: WGS 1984  
 false easting: 500 000.0000  
 false northing: 0.0000  
 central meridian: -9.0000  
 scale factor: 0.9996  
 latitude of origin: 0.0000  
 Units: Meter

## Work done at NDSSL - Virginia Tech

### Notes:

- Based on County Level ODE Model
- No demand on Sinje
- Minimal Demand on Bomi

### Sources:

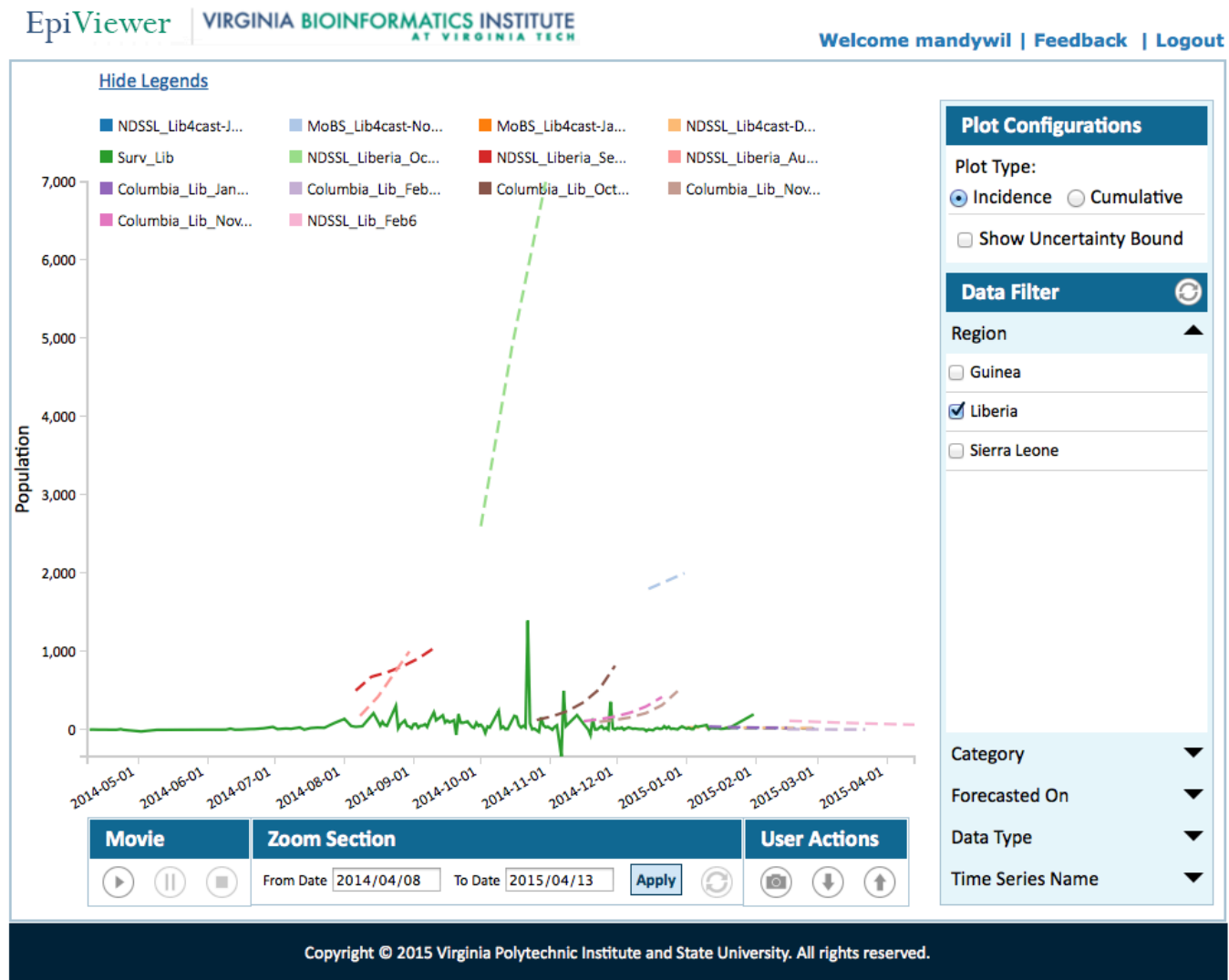
Pop: LandScan 2013  
 Roads: LISGIS (Eherton)  
 Rivers: DIVA-GIS



# EpiViewer



EpiViewer graphs Ebola surveillance and forecasting data from a variety of sources so trends and correlations may be made. Users can limit the graphs via a number of data filters, and they can also specify incidence or cumulative numbers. This data can be downloaded (either manually or by API.) While this tool was built specifically for Ebola, it can easily be extended to support other epidemics.





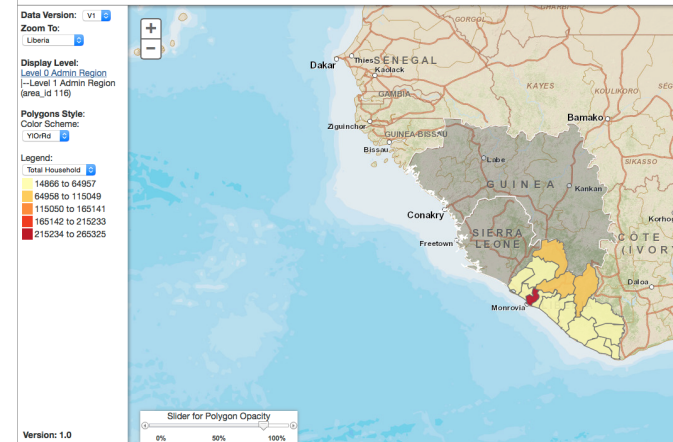
# Agent-based Modeling

## Synthetic Information Viewer (for Ebola Countries)

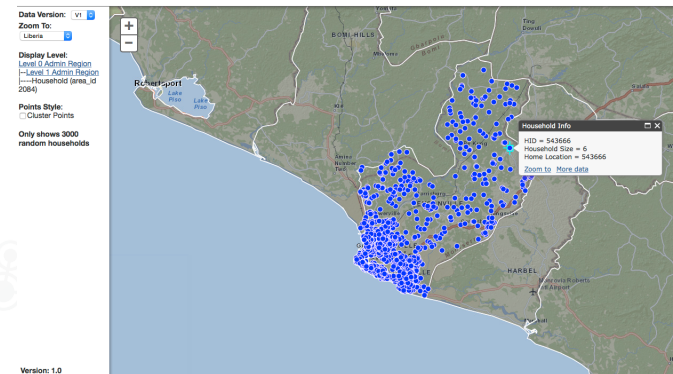


- Each individual represented, interactions drive transmission
  - Includes household, school, and work activities

## Synthetic Information Viewer (for Ebola Countries)



## Synthetic Information Viewer (for Ebola Countries)

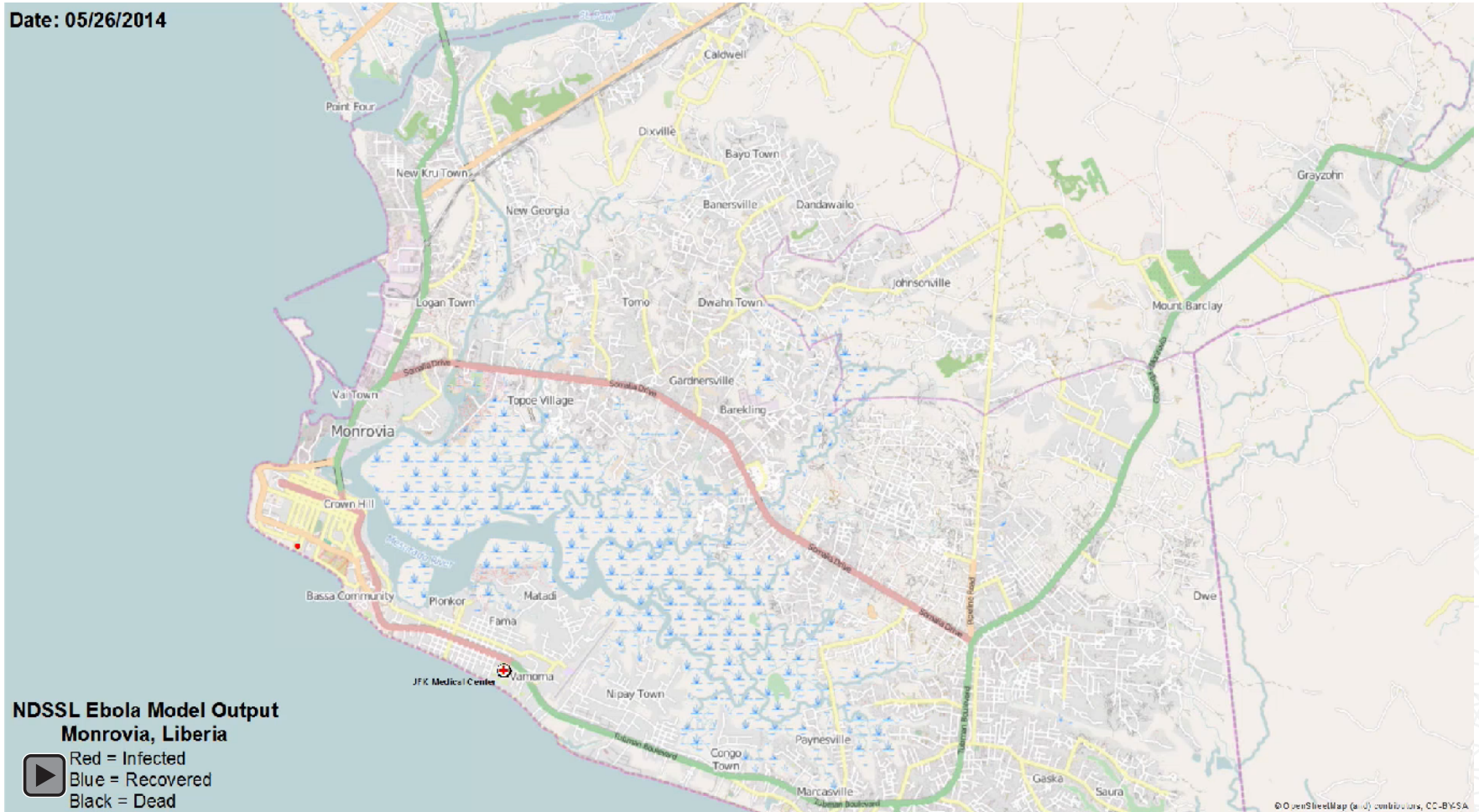






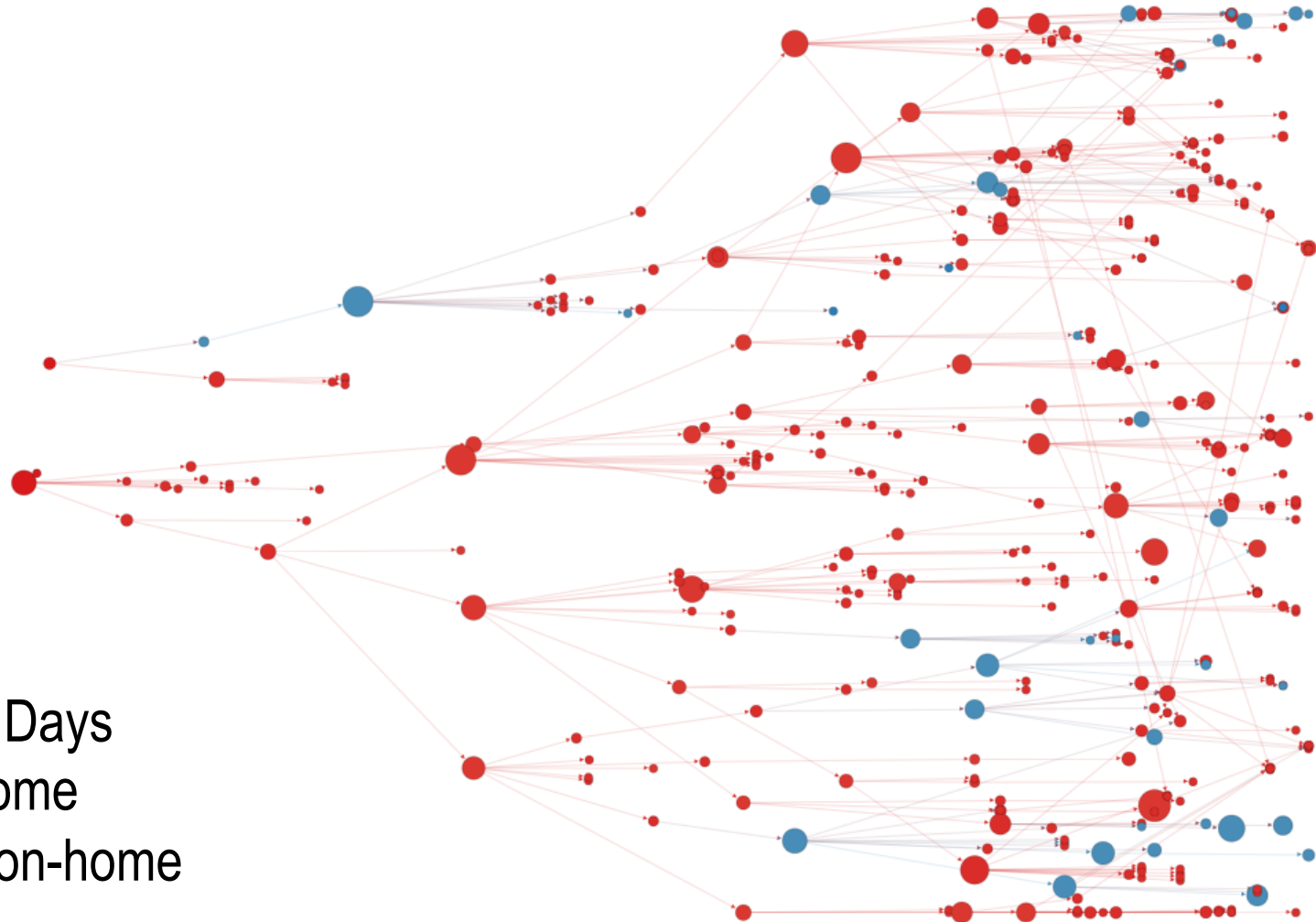
# Agent-based Modeling

Date: 05/26/2014





# Transmission Trees



X-axis is Days  
Red is home  
Blue is non-home





# On going Work

- Stochastic Extinction
  - Role of chance in initial spread and propagation of emerging diseases
- Complex Calibrations
  - Calibrating with multiple constraints (eg geo-spatial and temporal)
- Vaccine studies
  - Using detailed agent based studies to evaluate vaccine properties and guide design of field studies



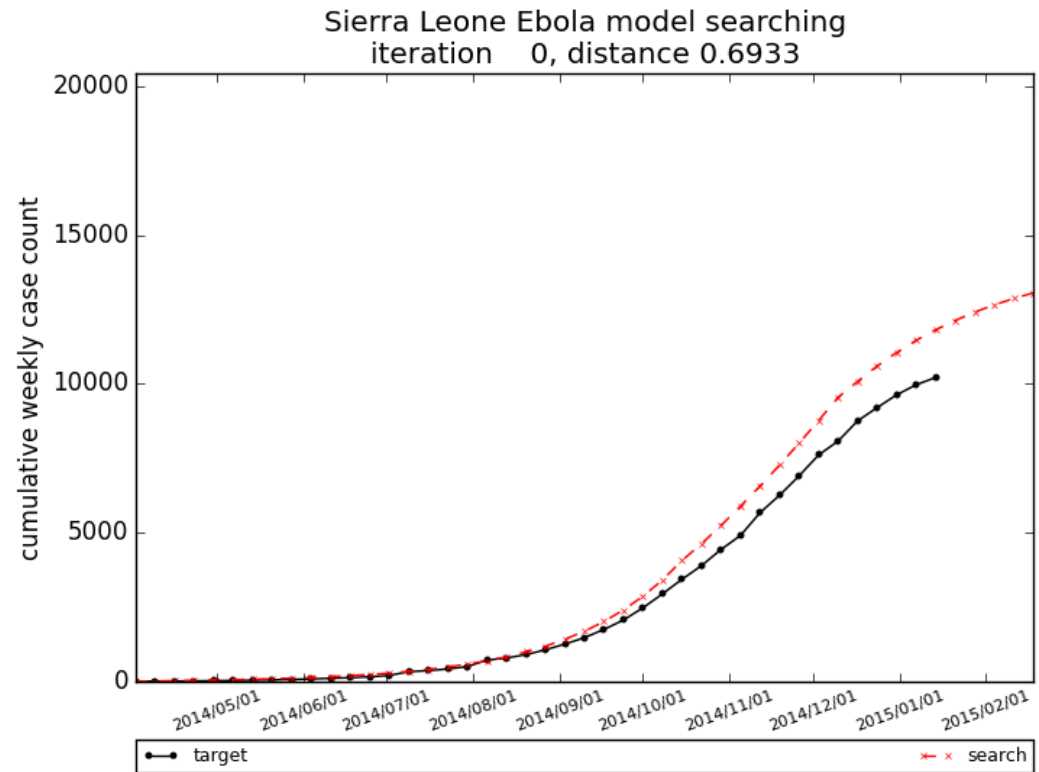
# Behavioral Adaptation

- Can we understand and estimate the impact of behavioral changes while the outbreak is on going?
- Details included in this ABM can provide a variety of structurally valid behaviors matching observations
  - These can be used to design field studies or epidemiologic analyses for confirming or disconfirming these behaviors
  - Can be used directly in estimating impacts, forecasting future cases, further exploring other counterfactuals



# ABM Calibration system

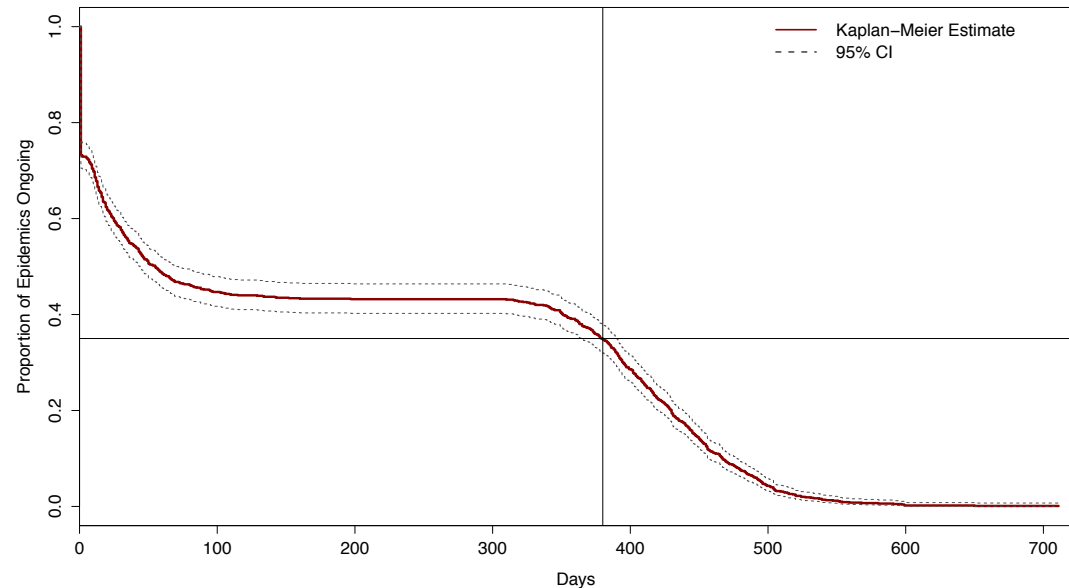
- Automated disease model / scenario search wrapped around full ABM simulations
- Use in upcoming RAPIDD Ebola forecasting Challenge





# Stochastic Extinction

- How likely is an outbreak of this size and kind?
  - Parameterize and calibrate model to observed values
  - Look at distribution of outbreaks produced (1000 sims)
- Prelim Results:
  - Same parameters that produce this outbreak produce many smaller ones and larger ones





# Vaccine Studies

- What are sufficient requirements of a vaccine and vaccine campaign to mitigate future outbreaks of this caliber?
  - Using parameters that generate large outbreaks roll out vaccine campaigns of various sizes, designs, and efficacy to estimate impacts
- Design of Vaccine trials greatly debated
  - Simulations assisted in evaluation of novel designs made to combat problem of declining incidence





# Summary and key insights

- Public health epidemiology is a complex system problem.
  - Responding to future pandemics challenging due to emerging global trends
  - Epidemics, contact networks, behaviors & policies coevolve during a pandemic
- Advances in computing & big data, have created new opportunities to support real-time epidemiology.
  - Simdemics: Network-based Computational Epidemiology -- Highly resolved, captures complex social and epidemic interactions
  - Role of multi-scale modeling and synthetic information
  - Leads to a qualitative change in the way public policies are supported
- Tools and experiences prove useful to prepare for the next outbreak



# Publications

Alexander K, Sanderson C, Marathe M, Lewis B, Rivers C, Shaman J, Drake J, Lofgren E, Dato V, Eisenberg M, Eubank S (2014)  
[What factors might have led to the emergence of Ebola in West Africa?. \*PLOS Neglected Tropical Diseases\*, 1418-1425.](#)

Rivers CM, Lofgren ET, Marathe M, Eubank S, Lewis BL.  
[Modeling the Impact of Interventions on an Epidemic of Ebola in Sierra Leone and Liberia. \*PLOS Currents Outbreaks\*. 2014 Oct 16. Edition 1.](#)

Lofgren E, Halloran M, Rivers C, Drake J, Porco T, Lewis B, Yang W, Vespignani A, Shaman J, Eisenberg J, Eisenberg M, Marathe M, Scarpino S, Alexander K, Meza R, Ferrari M, Hyman J, Meyers L, Eubank S (2014)  
[Opinion: Mathematical models: A key tool for outbreak response. \*Proceedings of the National Academy of Sciences \(PNAS\)\*.](#)

Rivers C, Alexander K, Bellan S, Valle S, Drake J, Eisenberg J, Eubank S, Ferrari M, Halloran M, Galvani A, Lewis B, Lewnard J, Lofgren E, Macal C, Marathe M, Mbah M, Meyers L, Meza R, Park A, Porco T, Scarpino S, Shaman J, Vespignani A, Yang W (2014)  
[Ebola: models do more than forecast. \*Nature\*, 515\(492\).](#)

Halloran M, Vespignani A, Bharti N, Feldstein L, Alexander K, Ferrari M, Shaman J, Drake J, Porco T, Eisenberg J, Valle S, Lofgren E, Scarpino S, Eisenberg M, Gao D, Hyman J, Eubank S, Longini Jr. I (2014) [Ebola: Mobility data. \*Science\*. 346\(6208\): 433.](#)

## **Previous Work:**

Alexander K, Lewis B, Marathe M, Eubank S, Blackburn J (2012)  
[Modeling of Wildlife Associated Zoonoses: Applications and Caveats. \*Vector-Borne and Zoonotic Diseases\*. 12\(12\): 1005-1018.](#)

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[Generation and analysis of large synthetic social contact networks. In \*Proceedings of Winter Simulation Conference \(WSC\)\*. 1003-1014.](#)



Thank you

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# Additional Slides