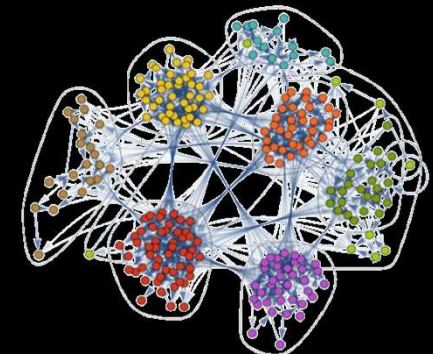


Exceptional service in the national interest



Building Confidence in Complex Systems Models for Reducing Population Health Risks

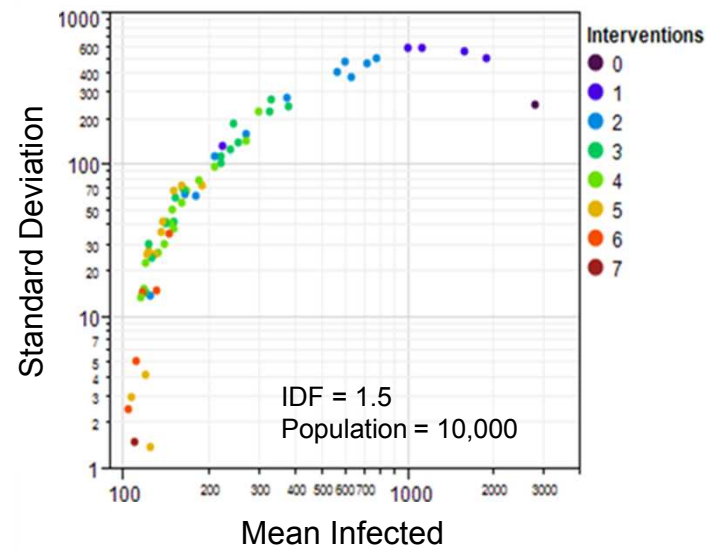
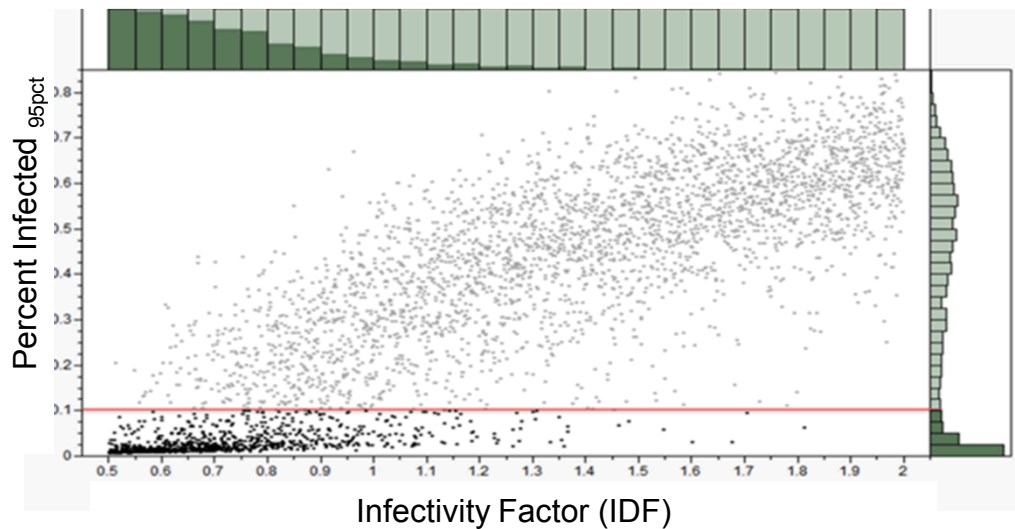
Theresa Brown
25 February 2016

Complex Systems Design & Management Asia 2016



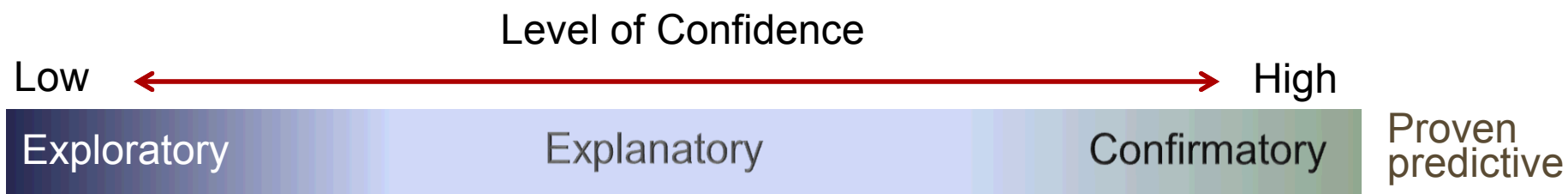
Key Takeaways

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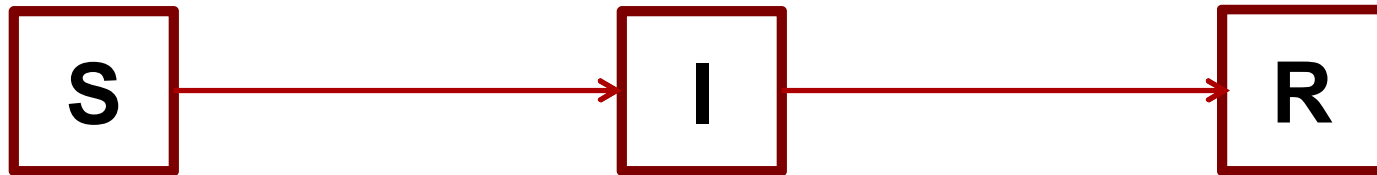
Epidemic Control: Central Analysis Questions

- *Scoping the potential damage:* What is the likely course of development for an outbreak if there is no intervention?
- *Guiding the response:* Which intervention strategies and associated resource deployments provide the best chance of success (fewest expected deaths, for example)?
- *Evolving the system:* How can we prevent future epidemics?

Observations

- **Heterogeneity** in the populations is important
 - Populations are not well-mixed
 - **Subpopulation level interaction structures** change over time
 - Mean-field approximation is not a suitable approach
- Individuals within the population **adapt**
 - To cope with disease spread
 - Due to interventions
- **System feedbacks** drive behaviors and disease spread
- These features are commonly observed attributes of complex systems

Hypothesis: epidemic control modeling can better inform development of intervention strategies by directly representing these Complex System attributes.



$$\frac{dS}{dt} = -\beta SI$$

$$\frac{dI}{dt} = \beta SI - \alpha I$$

$$\frac{dR}{dt} = \alpha I$$

Average Infected transmits infection to Susceptible with rate β

Infected Recover with average rate α

- Describe the population in terms of the number of members in each of a set of discrete states
- First introduced in 1927 (Kermack and McKendrick 1927)
- Several extensions (SEIR), including Legrand et al.'s (2007) Ebola model

Projection of Ebola Cases Using SEIR Models

- In September 2014, CDC released estimates of Ebola spread in Western Africa (Meltzer et al. 2014)
- Key findings include
 - Exponential growth without intervention
 - As many as 1.4M cases by January 2015
- Projections have been heavily criticized
 - “Avoidable errors in the modelling of outbreaks of emerging pathogens, with special reference to Ebola” (King et al. 2015)
 - WHO reported only 21k Ebola cases by January 2015
 - Concerns about misallocation of resources, “crying wolf”

Criticisms of SIR Models

- Omission: population adaptations not represented
 - Population will likely change structure of interactions and behaviors with notification of outbreak
- Assumption: well-mixed, homogeneous spatial distribution of population
 - Social contact structures that are central to disease propagation are not represented
 - Omission of interaction structures limits spectrum of control strategies that can be evaluated
- Meltzer et al. acknowledge several limitations with their estimates

“Spread of modern epidemics is spatially incoherent and chaotic, generically does not bear any metric regularity, and observed spatio-temporal patterns depend sensitively on the outbreak location”.

Helbing et al. 2015

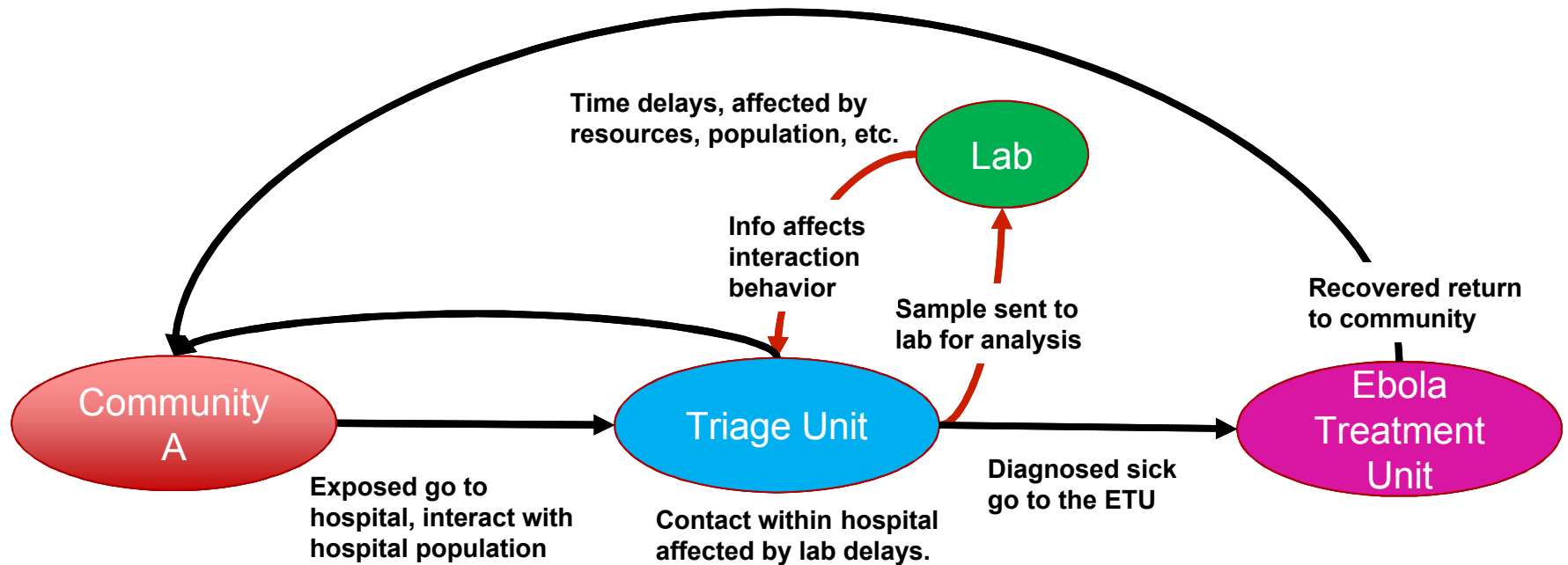
- Agent-based models of contact network control on disease have become common since 2007
 - Pros: network structure captures heterogeneity better than compartmental models
 - Cons: Insufficient data to parameterize network structure results in massive new uncertainties

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 - Widespread failure to predict disease patterns from very expensive models (e.g. 2009 H1N1)
 - Highly detailed simulations can be misleading when drive for more detail outpaces available information

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- Outcomes:
 - Widespread failure to predict disease patterns from very expensive models (e.g. 2009 H1N1).
 - Highly detailed simulations can be misleading when drive for more detail outpaces available information.
- **Needed:** Balanced approach which incorporates complexity better than compartmental models without uncertainty problems of “photo-realistic” disease spread simulations

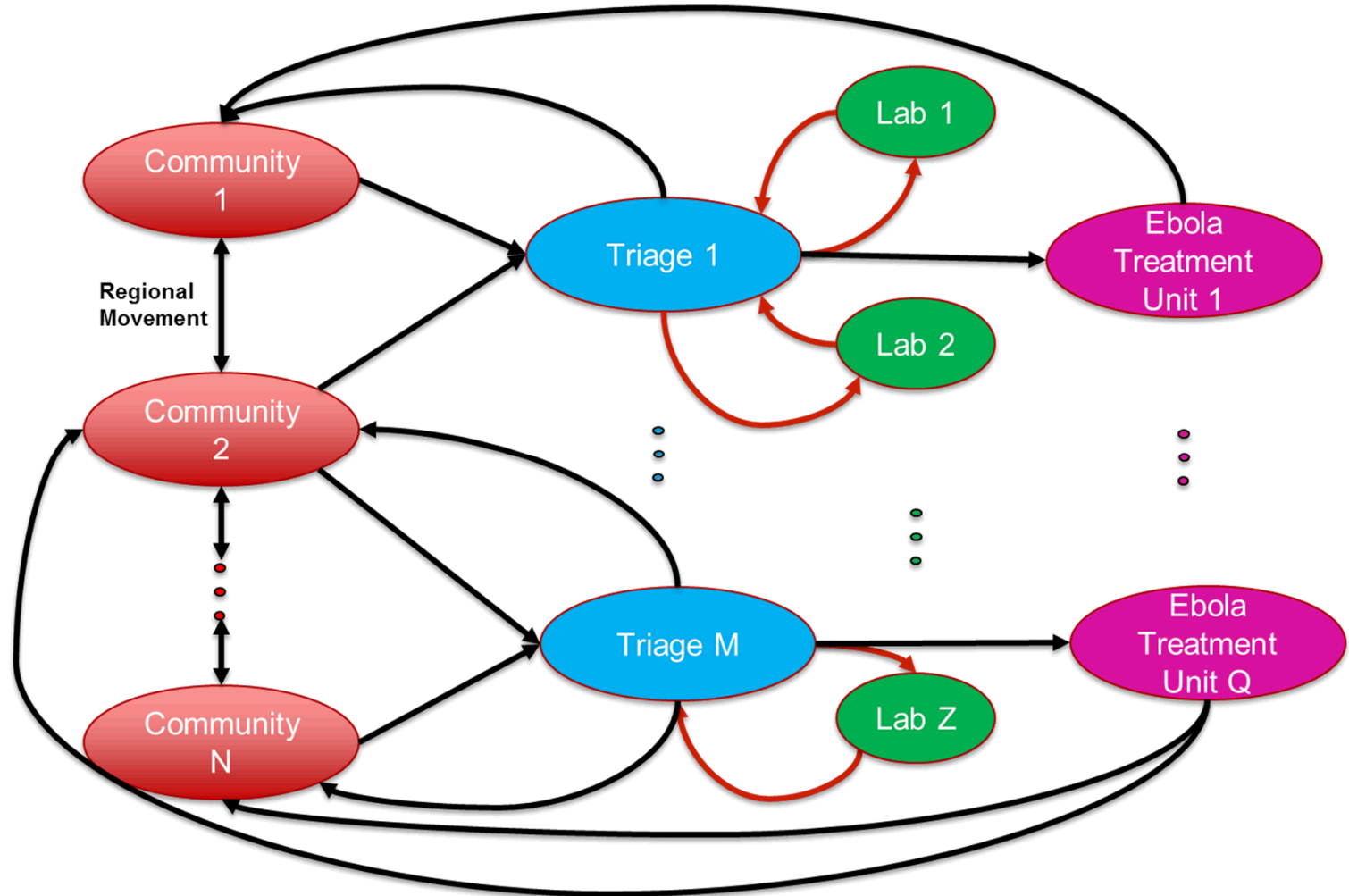
- Represent physical locations
- Represent interactions
 - Within location: SEIR formulation
 - Between locations: determined by interaction structures (e.g., regional movements, institutional controls)
- Represent adaptations and control strategies
 - Information flow affects behavior
 - Modify interaction structures (e.g., isolation)
 - Modify rate constants (e.g., analysis delays, transport times)

Conceptual Illustration



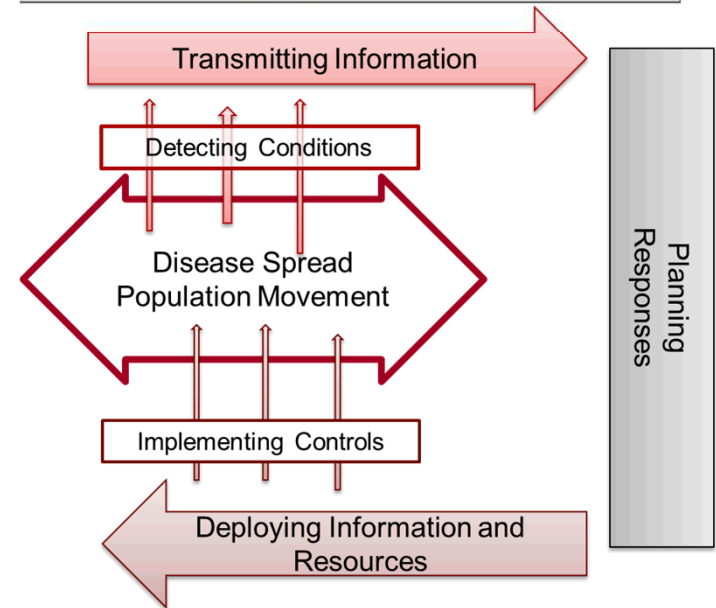
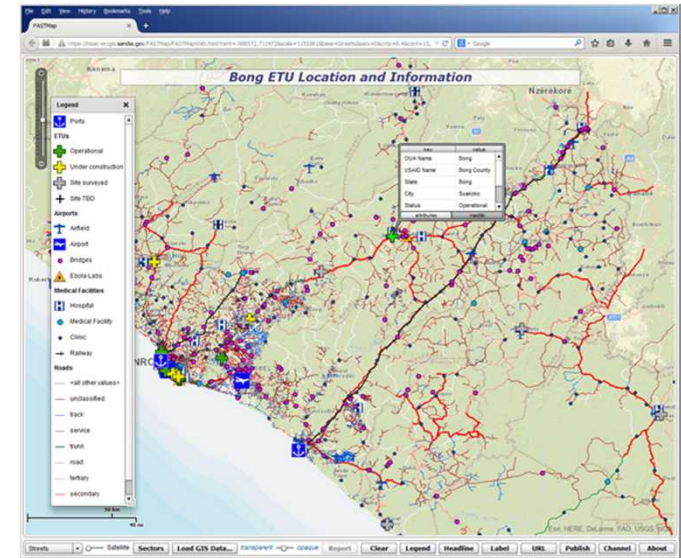
- People Flow
- Information Flow

Conceptual Illustration: Replicate Across Multiple Units



Conceptual Model Development: What is or could be important in Disease Control: Ebola Example

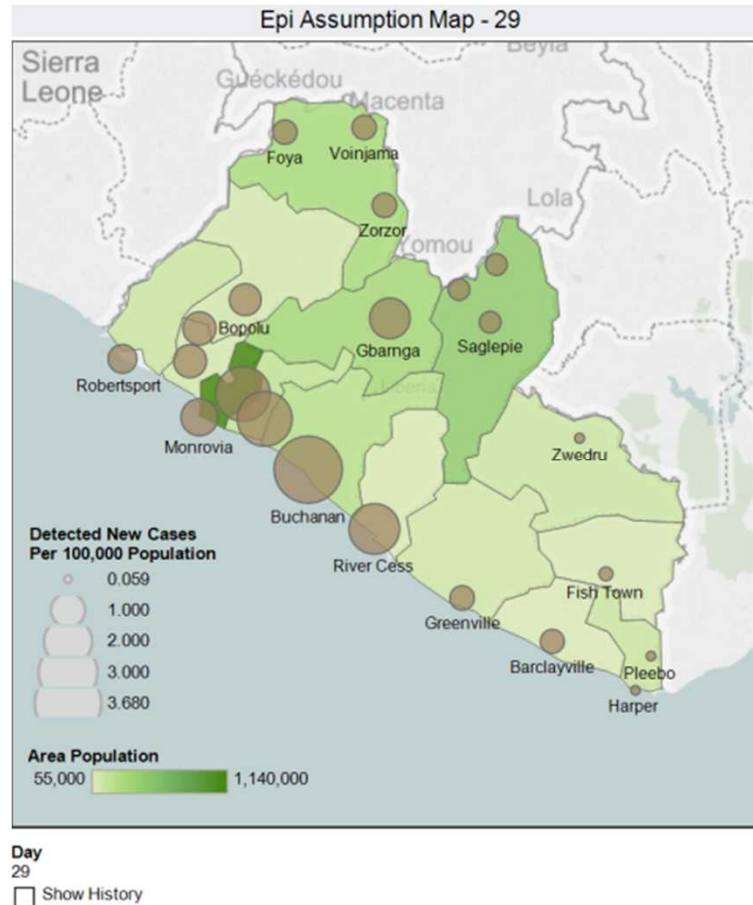
- State of knowledge (what is known):
 - Disease epidemiology
 - Incidences of disease at various locations
 - Population characteristics including: size and density
 - Important factors in disease spread include: contact networks, interactions and behavioral responses
 - Poor response was likely to lead to significant loss of life
 - Transportation routes and general conditions
 - Administrative limitations (curfew)
 - Lab locations and capacities
- Uncertainties (unknowns due to lack of data):
 - Extent of disease spread
 - Population movements, interactions and responses
 - Sample processing times
 - Which controls and resource deployment strategies will work best



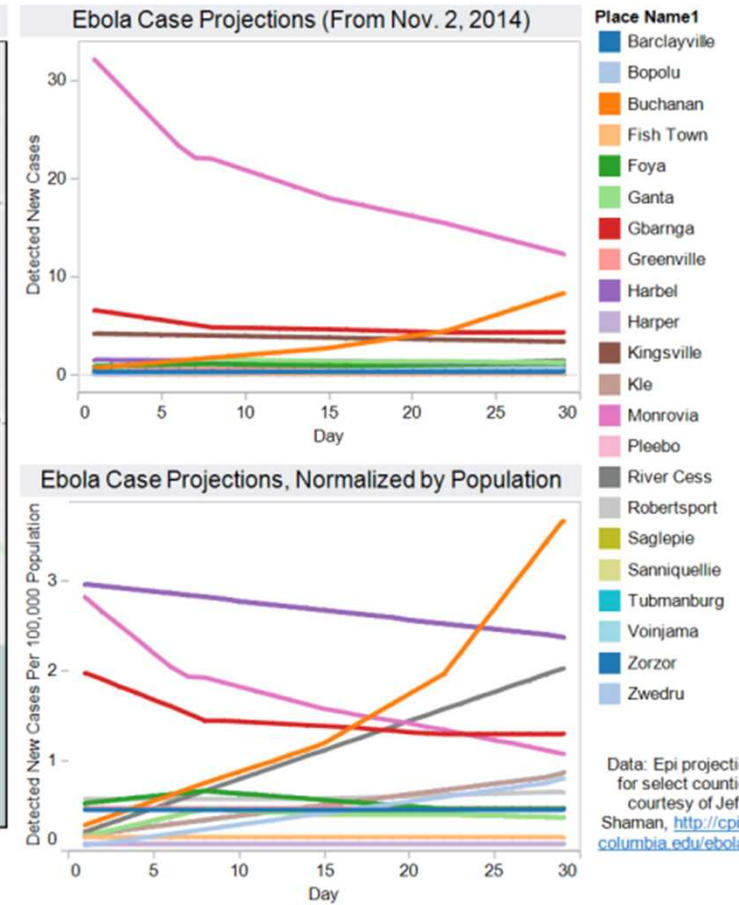
Ebola disease parameter values and initial conditions

Sierra Leone

Population and Reported Cases



Projected Cases



Disease Control: Ebola Test Scenario

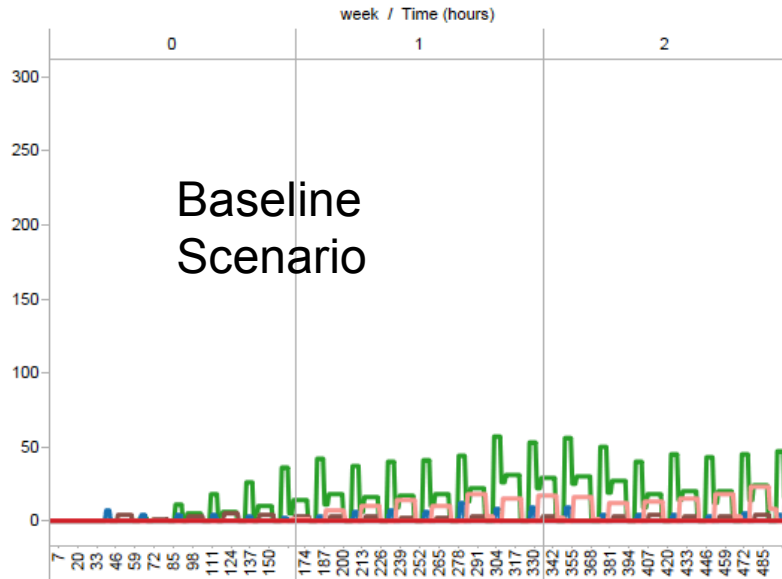
Labs: Samples Awaiting Testing

- Scenario ID
- Null
 - BaseInfBaseTT
 - Spot4InfBaseTT
 - Spot4InfRoute3b

Labs Dynamic
Samples Awaiting Testing

Hotspot scenario: disease outbreak in rural communities north of Monrovia, Robertsport, Tubmanburg, Klu area patients presenting at Sinje and Tubmanburg clinical facilities

Baseline Scenario



Induces overloading on Island Clinic laboratory

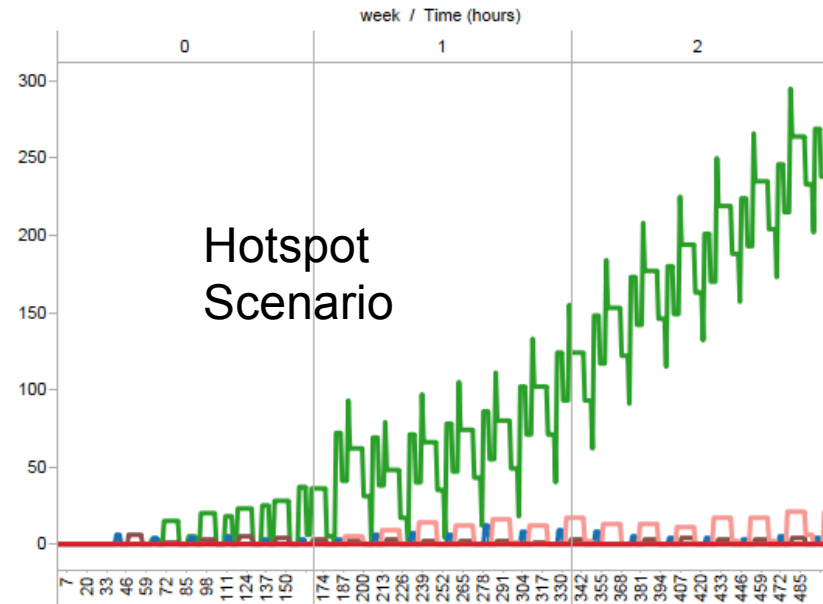
- Island Clinic receiving samples from northern communities and from within Monrovia

Labs: Samples Awaiting Testing

- Scenario ID
- Null
 - Spot4InfBaseTT
 - Spot4InfRoute3b

Labs Dynamic
Samples Awaiting Testing

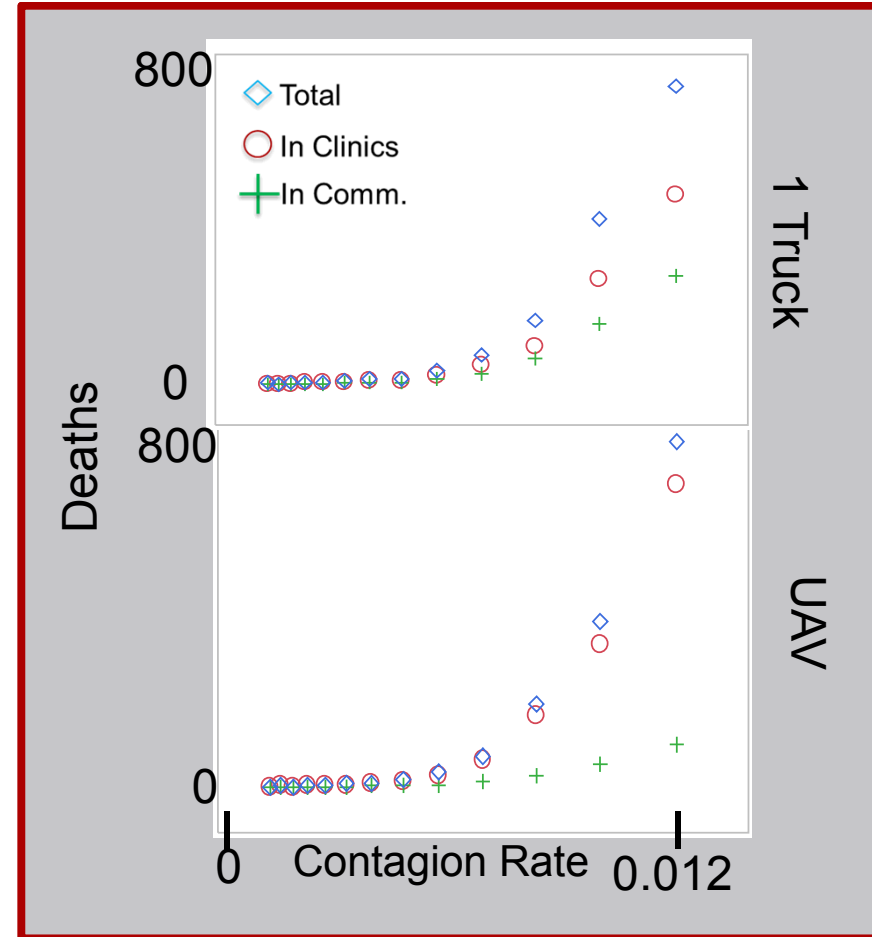
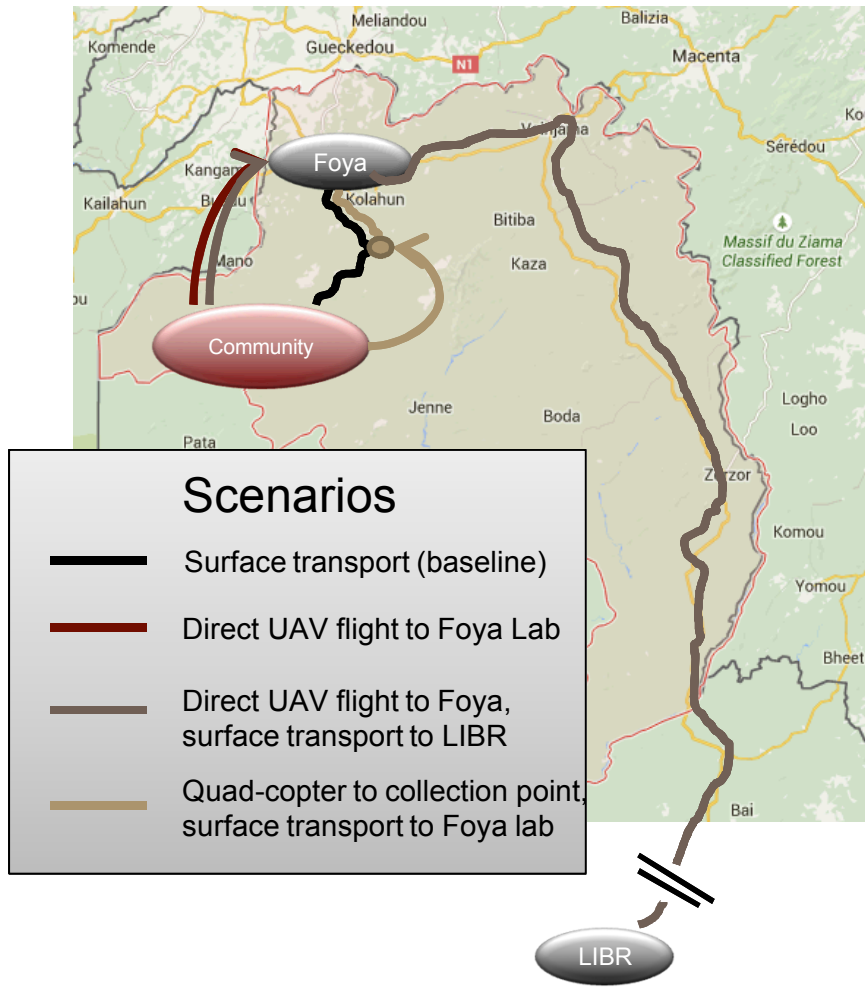
Hotspot Scenario



Lab Name

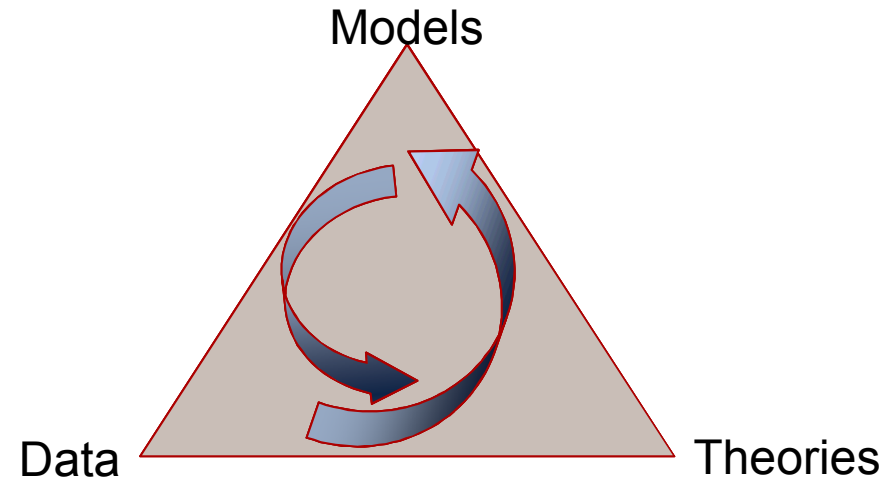
- CDC NIH ELWA Team 2
- MSF ETUc in Foya
- USN NMRC Gbarnga Lab Team 1
- MOH USAMRID Kakata
- NEW Fish Town Lab
- USN NMRC Island Clinic Lab Team 2

Example Analysis: Ebola Sample Collection and Transport



Technical Challenges

- Data
- Quantifying data quality, model bias and parameter uncertainty
- Modern sensitivity and uncertainty analysis methods operate on summary scalar outputs while CS models capture processes through time-series data outputs
- Huge numbers of runs required for multivariate testing



Immediate Research Needs:

- Identifying what is observable and measurable in complex systems
- Categorizing complex systems by their structure, predictability and susceptibility to control
- Developing and testing single-value output that adequately characterize time-series complex system outputs

Takeaways

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