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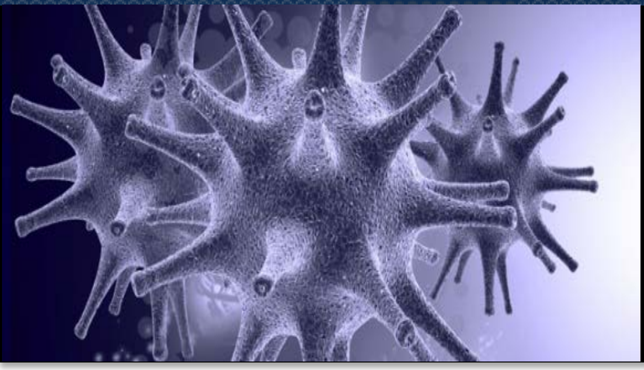

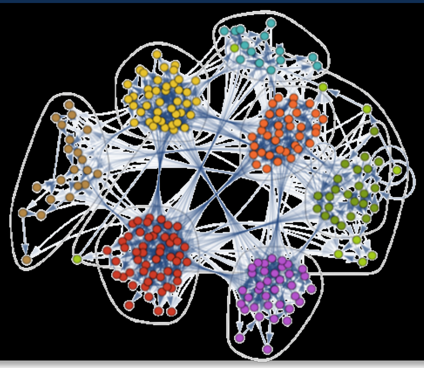

Building Confidence in Complex Systems Models for Reducing Population Health Risks

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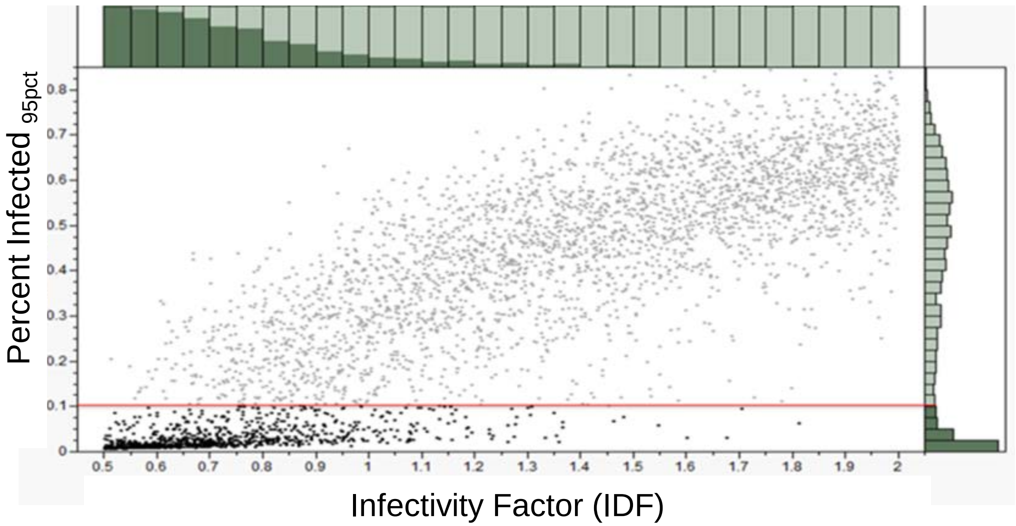
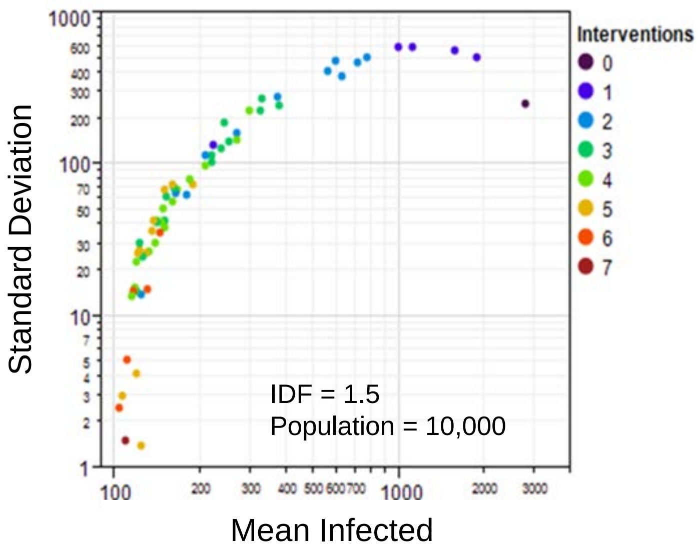
Key Takeaways

- *Experiment with models before implementing strategies in the real system*





References:

- ***Health Outcomes and Costs of Community Mitigation Strategies for an Influenza Pandemic in the United States***, Daniella J. Perlroth, Robert J. Glass, Victoria J. Davey, Daniel C. Cannon, Alan M. Garber, and Douglas K. Owens. Clinical Infectious Diseases, vol. 50, no. 2, p. 165-174. Expedited publication. January 2010 PubMed Summary
- ***Effective, Robust Design of Community Mitigation for Pandemic Influenza: A Systematic Examination of Proposed U.S. Guidance***, Robert J. Glass, Victoria J. Davey, H. Jason Min, Walter E. Beyeler, and Laura M. Glass. PLoS One, vol. 3, no. 7. July 2008 (2008-0561 J)

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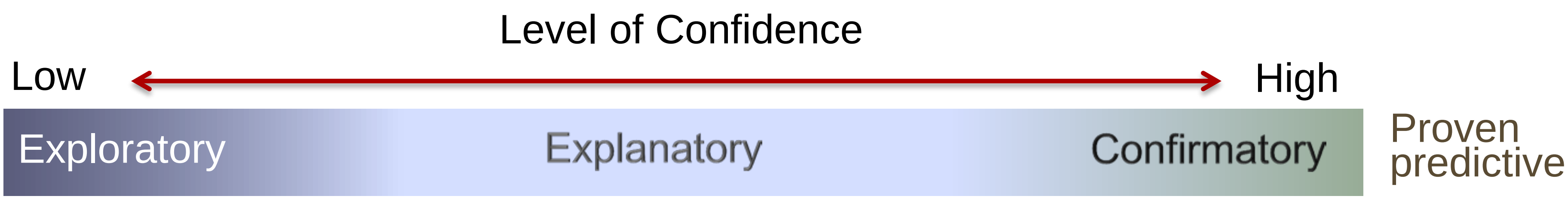
- *Experiment with models before implementing strategies in the real system*
- *Ambitious but realistic goals for CS models are that they be explanatory and through experimentation and data collection we develop a medium-level of confidence in their predictive capability*



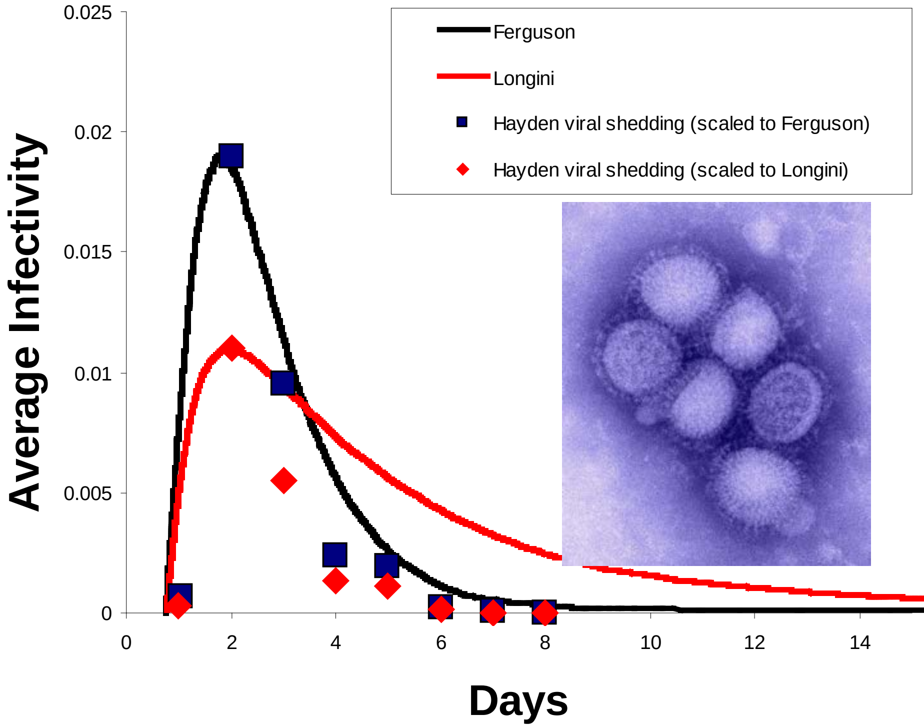
Key Takeaways

- *Experiment with models before implementing strategies in the real system*
- *Ambitious but realistic goals for CS models are that they be explanatory and through experimentation and data collection we develop a medium-level of confidence in their predictive capability*

- *It will take a global community of practice to achieve these goals*

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?



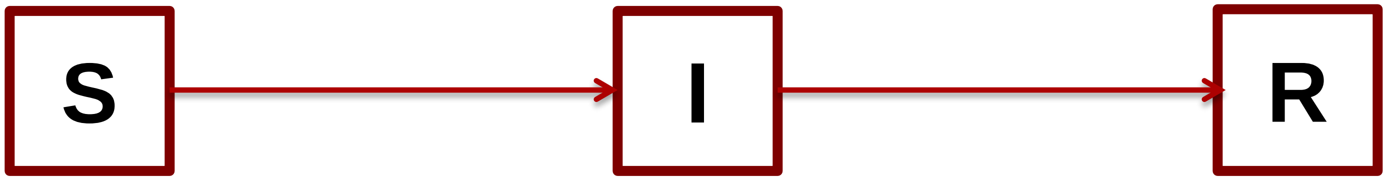
Average population scale infectivity for Ferguson and Longini-like disease manifestations with viral shedding data from Hayden (Hayden, Fritz et al. 1998) scaled to the peak infectivity.

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.

Standard Approach – Compartment Models



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

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 at el. 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"

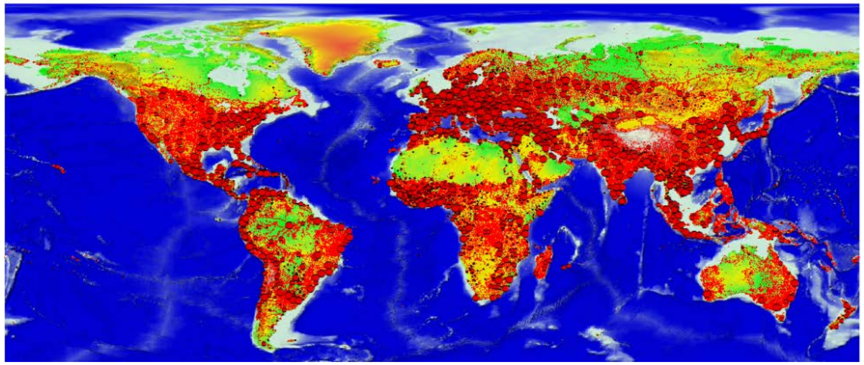
Criticisms of SIR Models

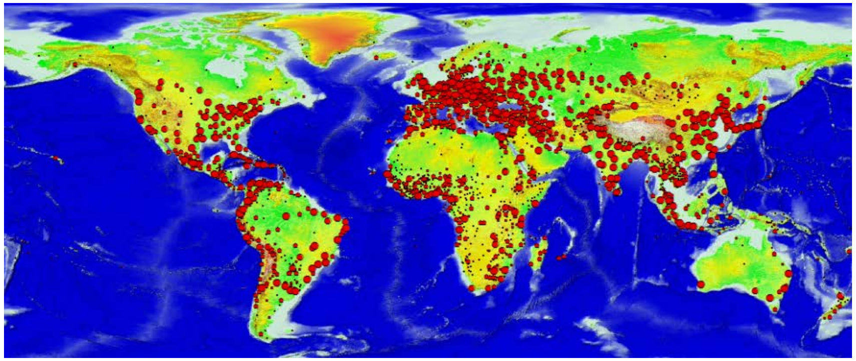
- Omission: population adaptations not represented
  - Population will likely change structure of interactions and behaviors with notification of outbreak
- Assumption: well-mixed, homogeneous spatial distribution of population
  - Social contact structures that are central to disease propagation are 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
> Journal of Statistical Physics

Detailed Networks without Supporting Data

- 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





Detailed Networks without Supporting Data

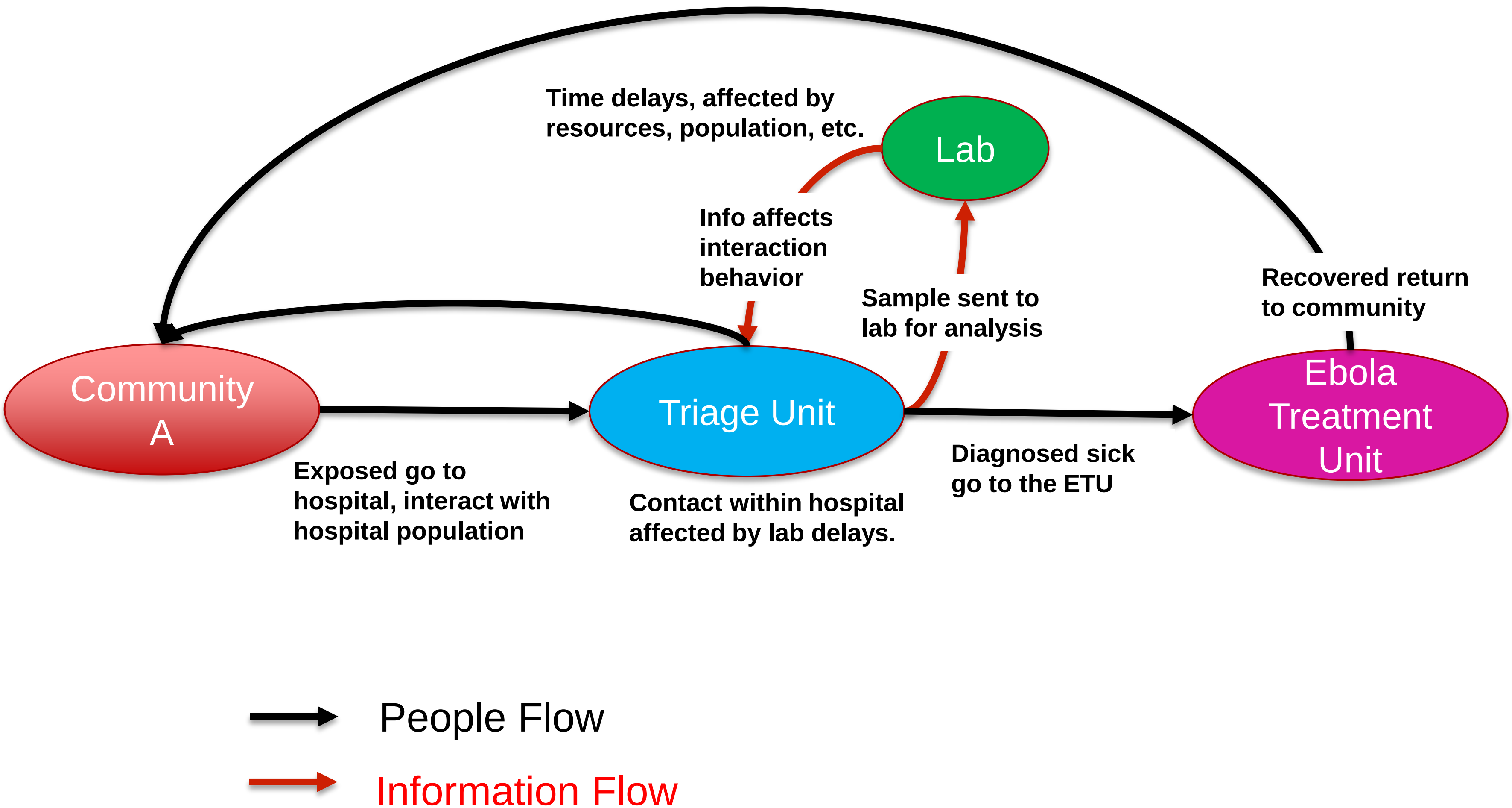
- Agent-based models of contact network control on disease have become common since 2007
  - Pros: network structure captures heterogeneity better than compartmental models
  - Cons: Insufficient data to parameterize network structure results in massive new uncertainties
- Outcomes:
  - Widespread failure 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: A balanced approach which incorporates complexity better than compartmental models without uncertainty problems of "photo-realistic" disease spread simulations

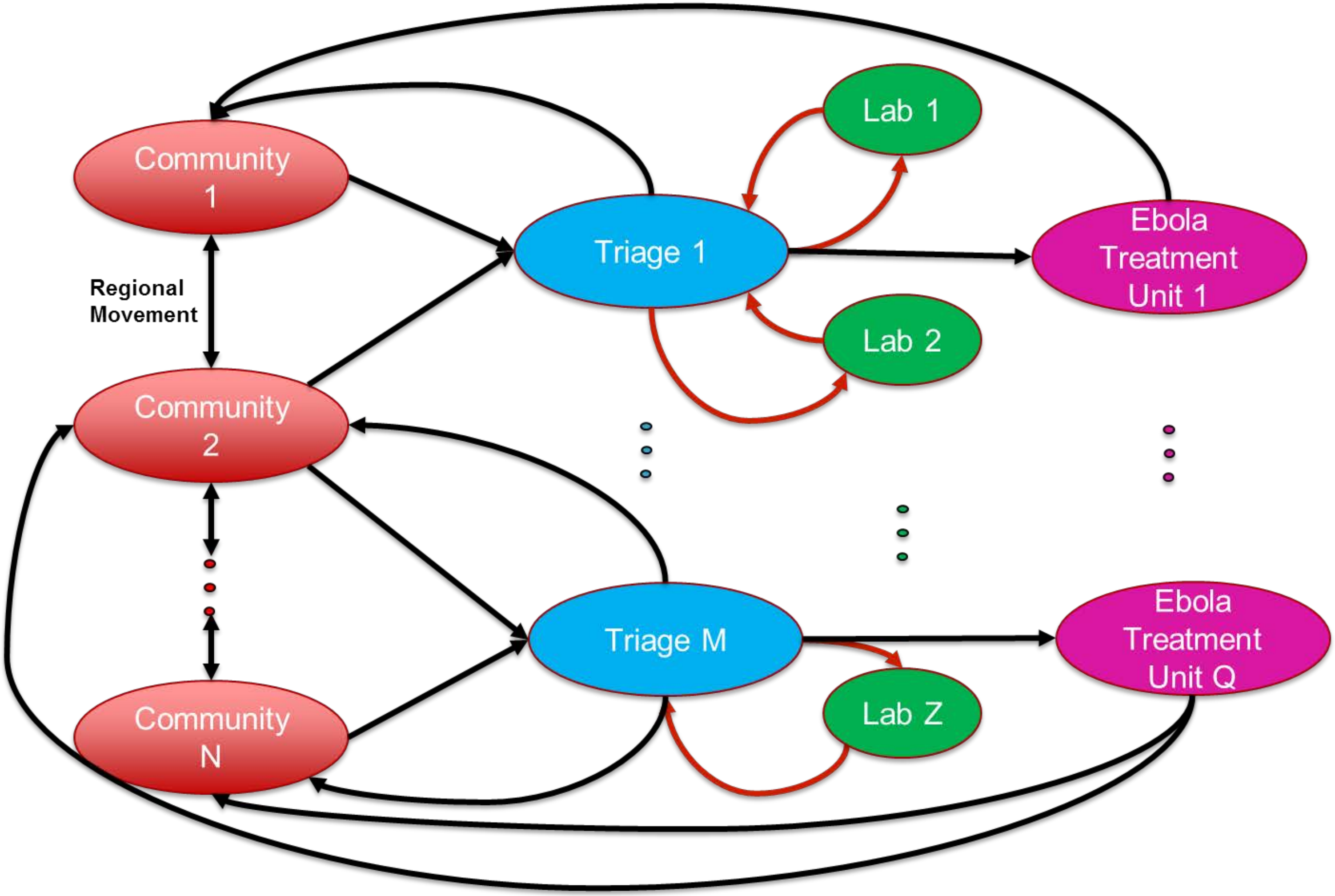
Sandia's Hybrid Approach

- 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



Conceptual Illustration: Replicate Across Multiple Units



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

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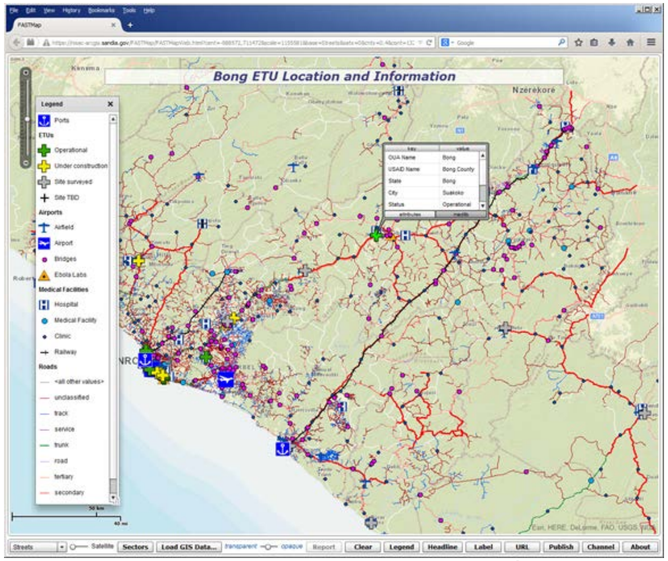
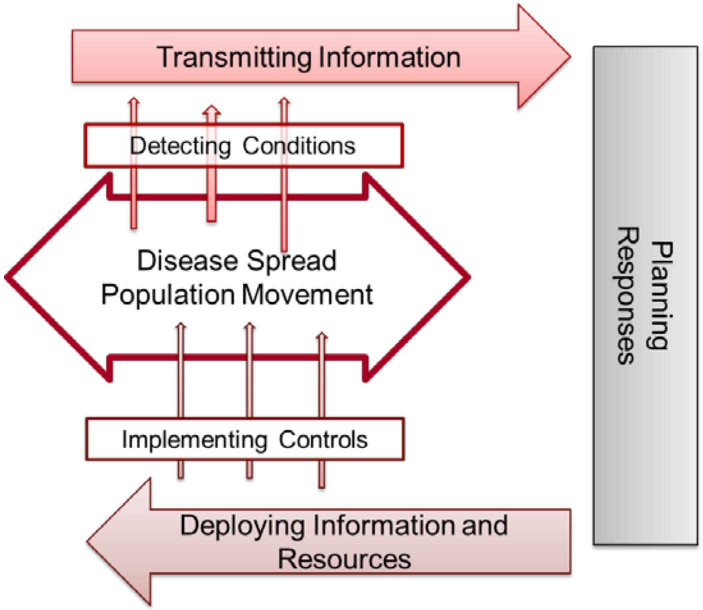
- State of knowledge (what is known):
  - Disease epidemiology
  - Incidences of disease at various locations
  - Population characteristics including: size and density
  - Important factors in disease spread include: contact networks, interactions and behavioral responses
  - Poor response was likely 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

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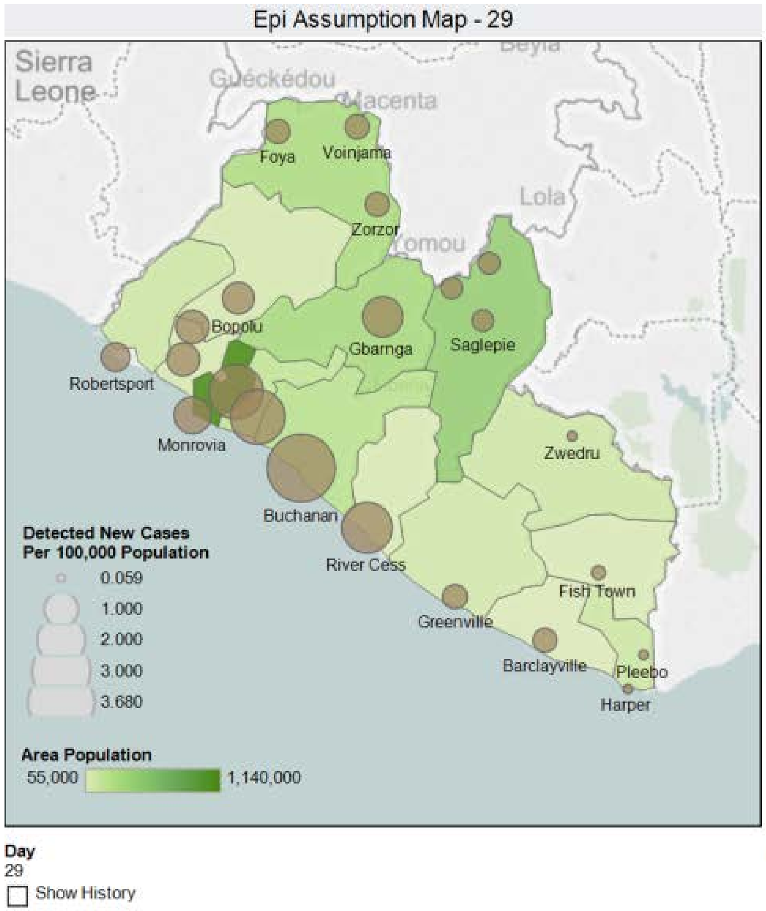
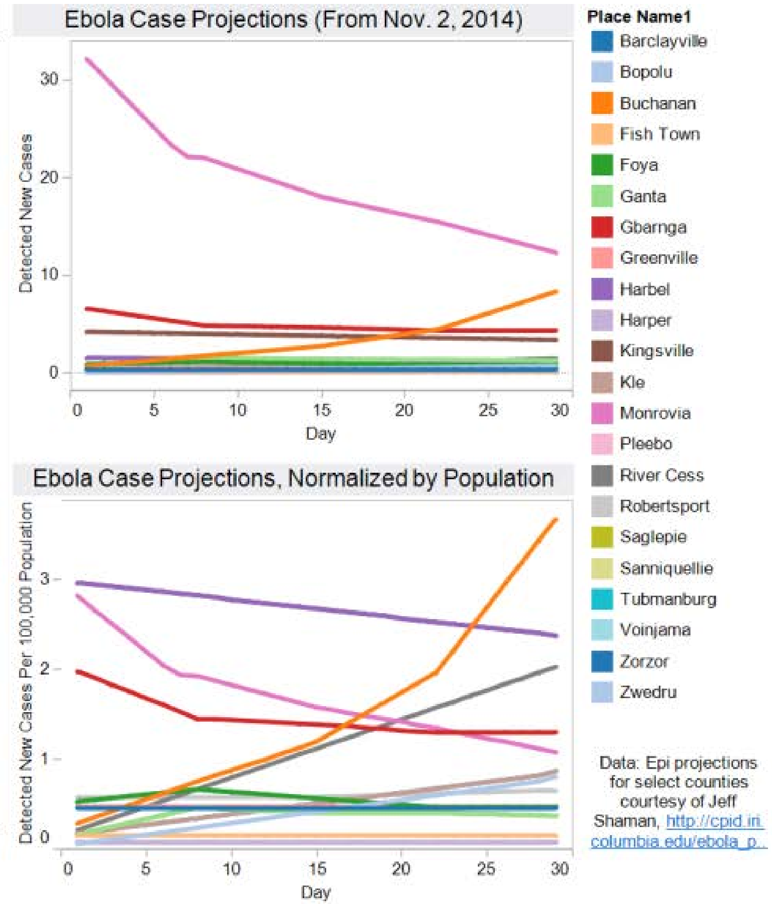
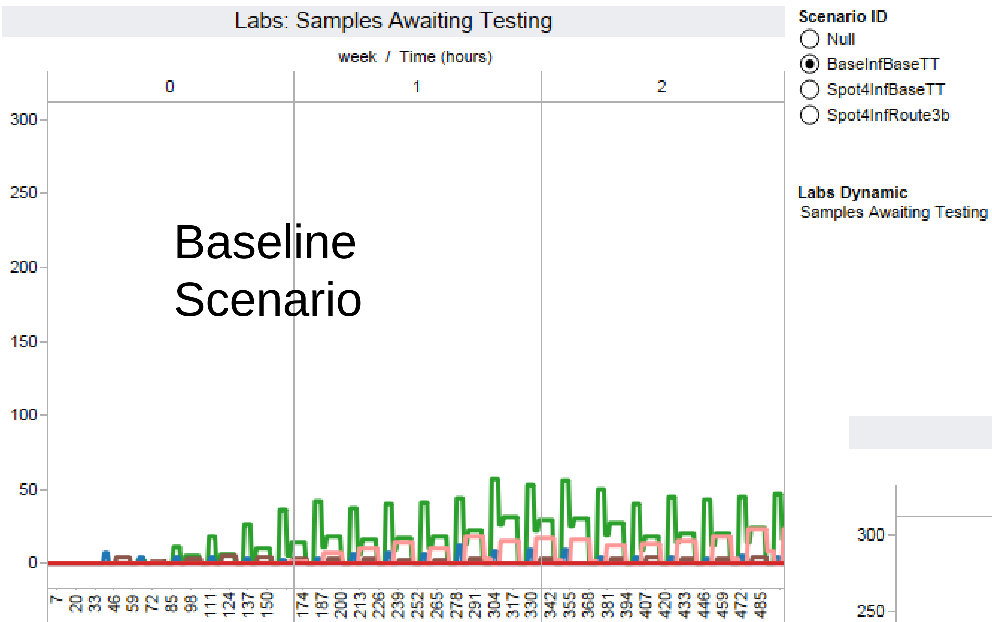
Population and Reported Cases



Projected Cases



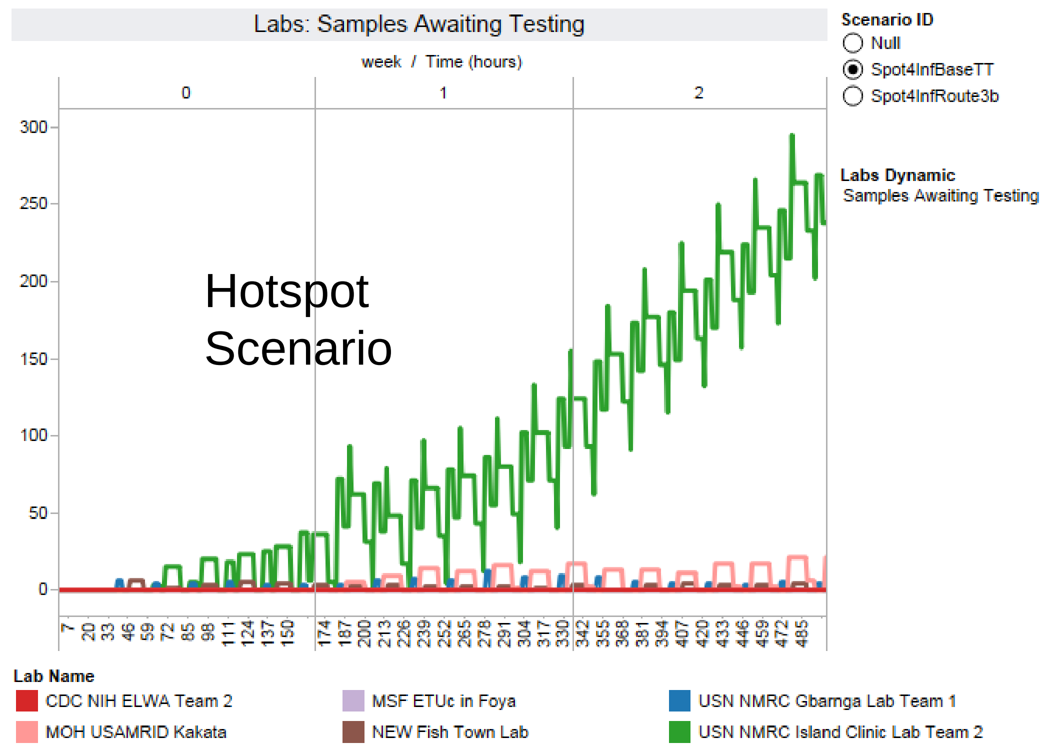
Disease Control: Ebola Test Scenario



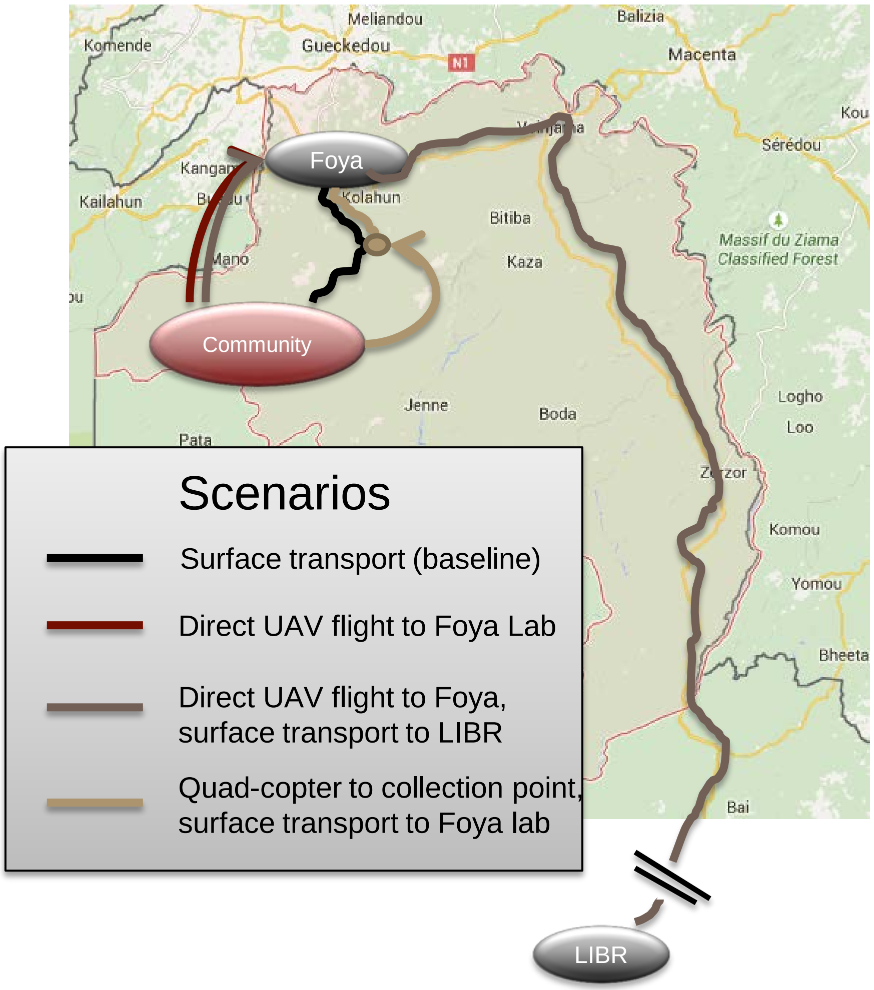
Hotspot scenario: disease outbreak in rural communities north of Monrovia , Robertsport, Tubmanburg, Klu area patients presenting at Sinje and Tubmanburg clinical facilities

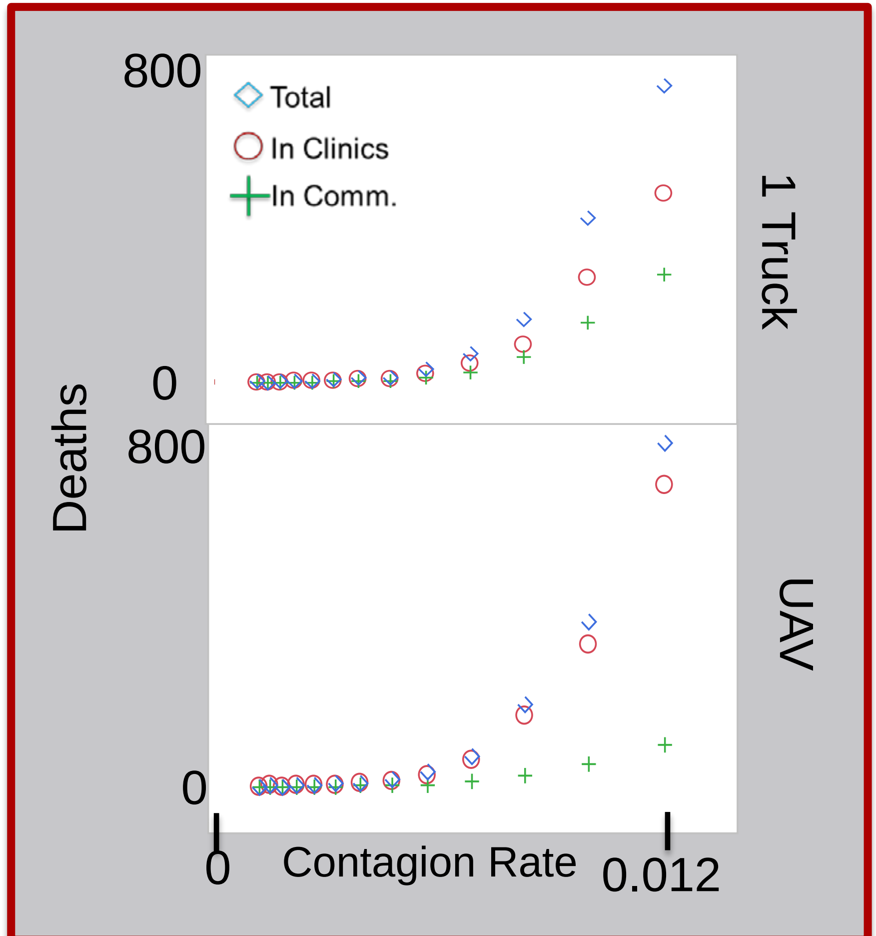
Induces overloading on Island Clinic laboratory

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



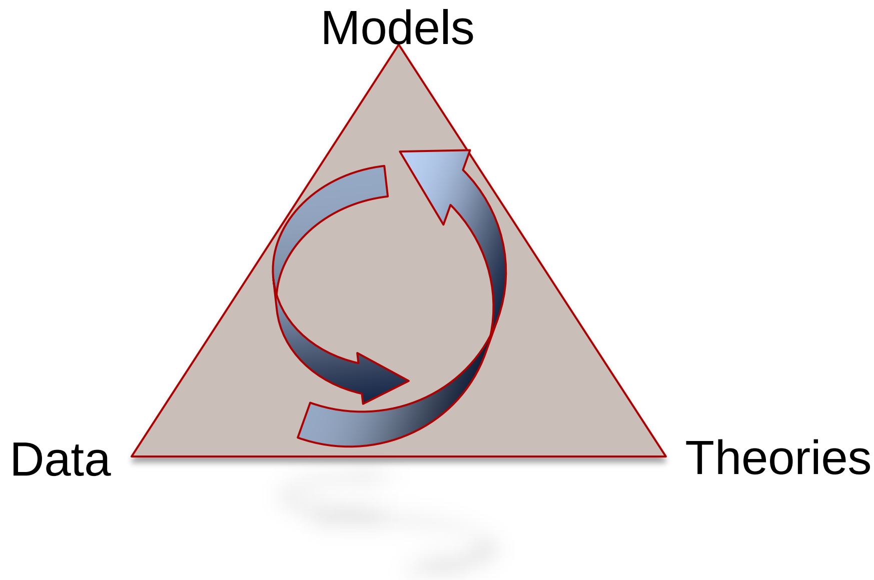
Example Analysis: Ebola Sample Collection and Transport





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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For more information and publications see:
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