Statistical Techniques for the Characterization of Partially Observed Epidemics

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Problem Statement

- **Aim: To develop statistical techniques to characterize *ongoing* epidemics from partial *biosurveillance* data**
  - **Estimate # of index cases, time of infection, or infection rate**
  - **Do so with minimal data i.e., early in the outbreak**
    - **Data is a time-series of counts of ICD-9 codes**
  - **Quantify the confidence in the estimates**
- **Motivation**
  - **To provide initial conditions for disease models, to be used for planning medical interventions, resource allocation etc.**
    - **Disease models can be agent-based ones too**
  - **Can also be applied to historical epidemics, with case-counts as the data**
    - **Useful for obtaining disease model parameters for agent-based simulators.**

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Why Are Current Biosurveillance Methods Inapplicable?

- Current *biosurveillance* methods focus on detection
  - Based on anomaly detection
  - No model of the background
    - Or filtered out and this "disturbs" the detection

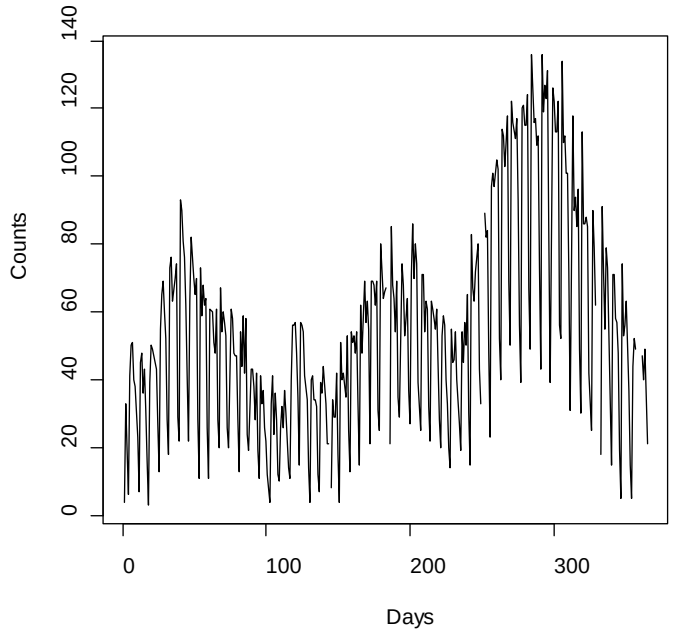
"7 day moving average filters suppress exactly the short scale features that were the intended object of study"

- *Bloom, Buckeridge, and Cheng, JAMIA (2006)*

- Current *characterization* methods for epidemics are used retrospectively
  - The epidemics are *fully* observed, not *partially* observed
  - The identity of the disease is known
  - The data consists of counts of people who have been diagnosed with the disease
    - It is *not* biosurveillance data with all its confounding issues

Difficulties with Using Biosurveillance Data

- **Biosurveillance data (ICD-9 counts, OTC sales etc) is complex**
  - **Weekly & seasonal cycles; non-stationary structure**
  - **Symptom, not diagnosis, data (for timeliness)**
- **Characterization of epidemics with biosurveillance data requires:**
  - **Ability to model the background/endemic morbidity in real time**
  - **Detect the start of the epidemic**
  - **Extract the epidemic from the data**
    - **By "subtracting" the background**



ILI ICD-9 stream from Miami (background / endemic morbidity)

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Technical Challenges

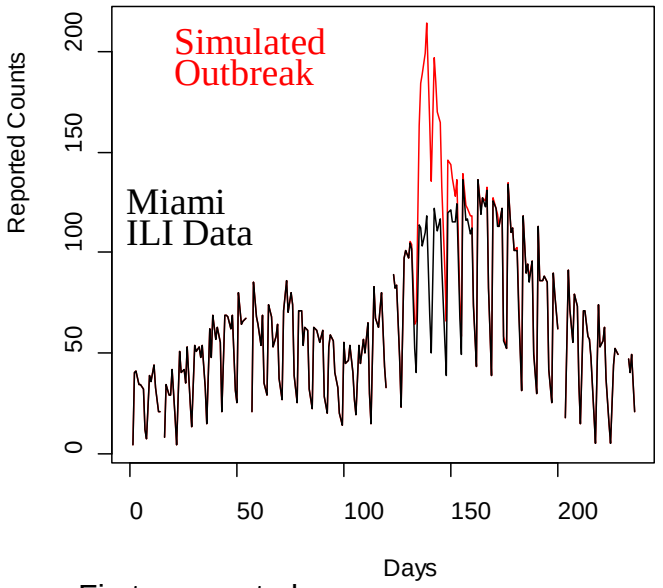
- The components of the procedure are:
  - *Detection* of an outbreak from time-series data
  - *Extraction* of the outbreak from the background
    - Data for detection and extraction are ICD-9 streams with both the background/endemic and outbreak signal
  - *Characterization* of the outbreak (index cases, infection rate …)
- Biosurveillance data is partial, so …
  - All estimates are uncertain, and
  - The uncertainties need to be quantified
- Figures of merit
  - Delay between infection and detection
  - Cleanliness of the separation of background and epidemic
  - Closeness of inferred and true nature of outbreak

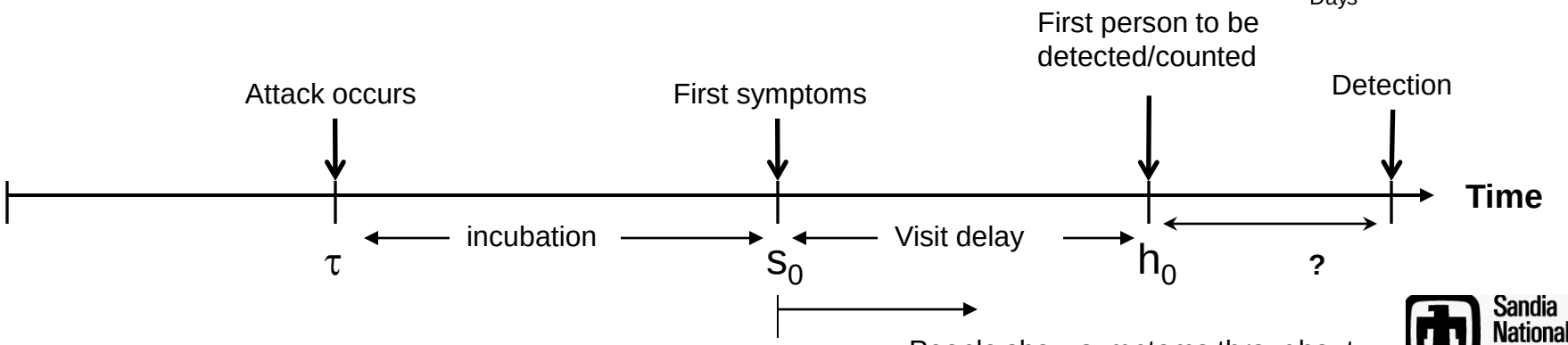
Detection of the Outbreak

- Based on sequential data assimilation using a Kalman Filter (KF)
  - Uses a simple model for daily ICD-9 counts (case-count)
  - Case-count model contains
    - A daily mean level and a cyclic weekly term
    - A quadratic, fitted to 4-week window of daily levels, for one-step-ahead predictions
  - KF also produce a measure of uncertainty in model predictions
    - KF covariance matrix
- Results in a model for the background morbidity
- Detection strategy:
  - Predict one-day ahead using quadratic model
  - If observation is greater than threshold, alarm (2-3 Std. Dev.)
  - Else, assimilate observation to obtain new mean level

Example with Synthetic Data

- **Simulated anthrax outbreak**
  - **Small atmospheric release over a spatially distributed population (3 Million people)**
  - **1125 index cases, with a range of doses**
  - **Includes visit delay**
- **Background data for Miami (ICD-9 for ILI)**
  - **Anthrax outbreak injected in on Day 130**
- **KF starts fitting background model from Day 0**
- **Question: How good is the background model**
  - **i.e. how many days to detection?**





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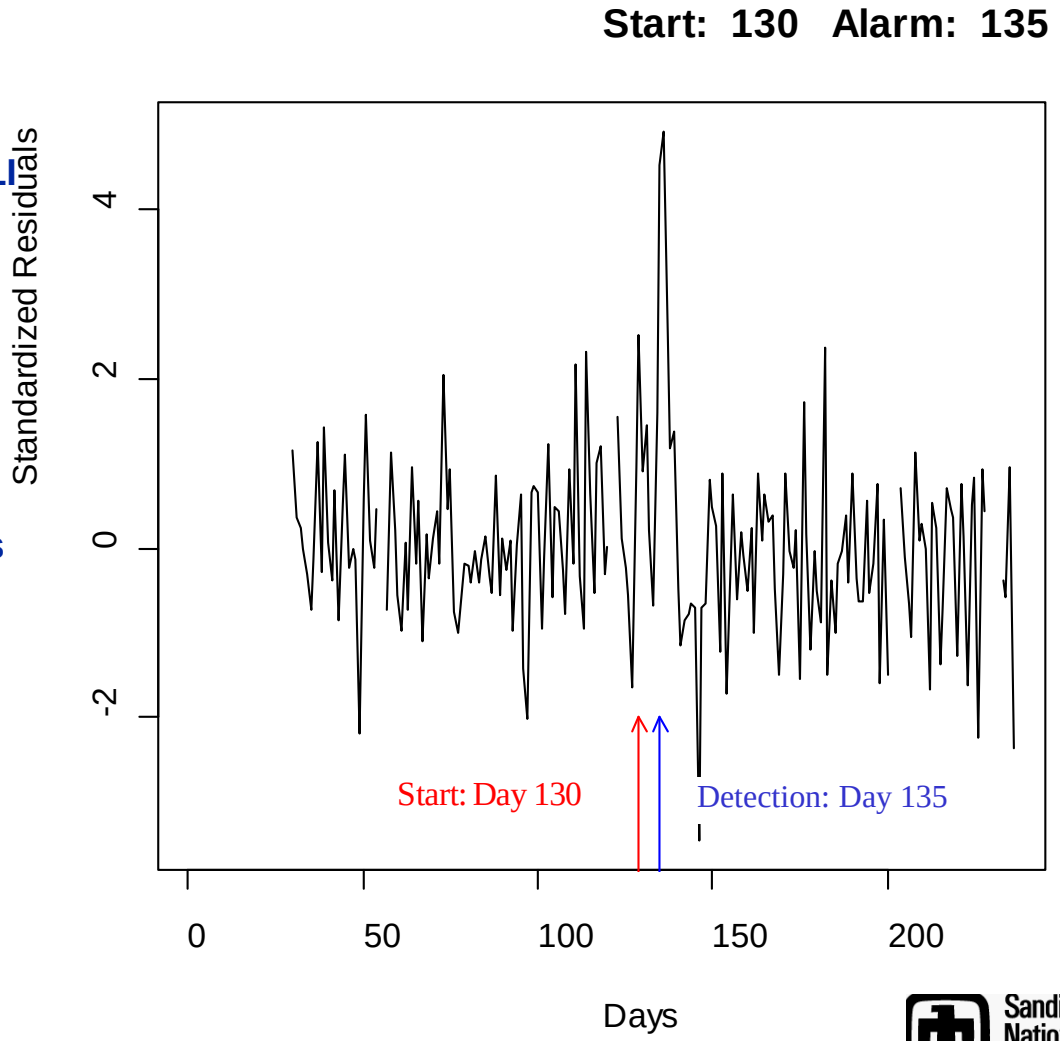
Detection Performance

- **Based on Kalman Filters**
  - Starts on Day 0
  - Creates a model of endemic ILI disease
- **Detection:**
  - One-day-ahead model predictions
  - Compared with observations
  - Significant deviation indicates an anomaly – detection!
  - In this case, detection took 5 days
  - Incubation: 3-4 days



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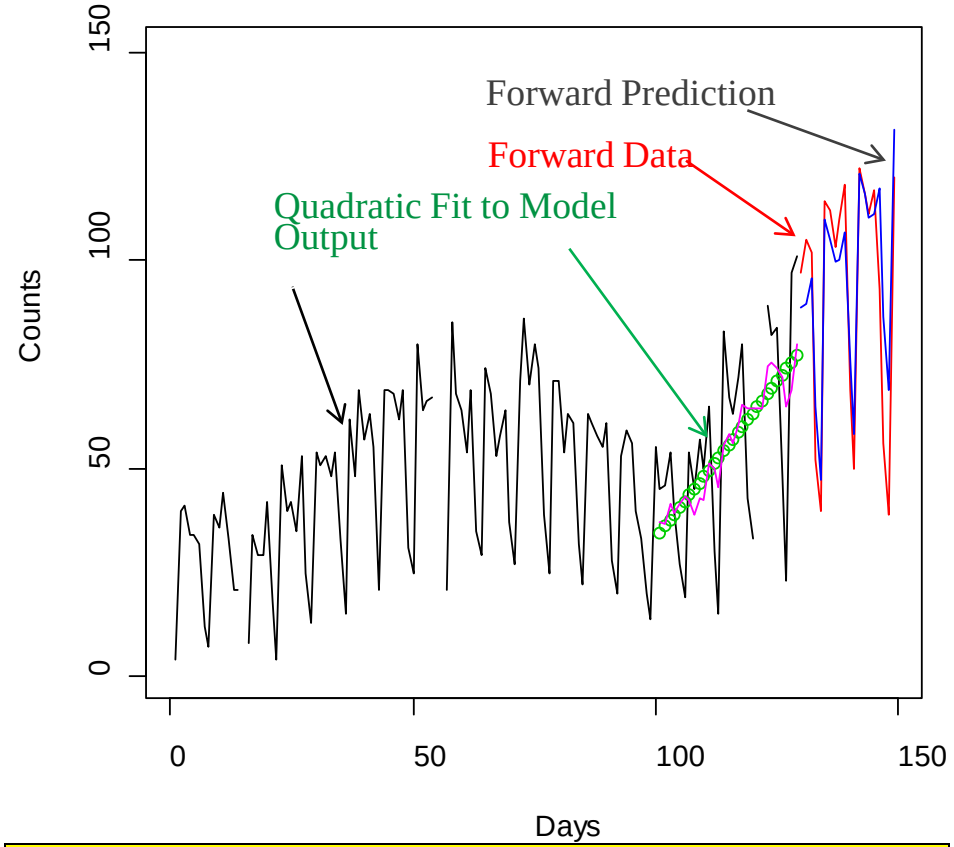
Extraction of the Epidemic

- The "background" model can be "frozen" on the day of alarm
  - A quadratic is fitted to mean levels to determine local slope for forward projection
  - Weekly cycles derived previous data
  - KF formalism used for forward projection
- Questions:
  - How close are the model predictions to observations?
- Test this without the injected outbreak.
- Caveat: Model predictions will degrade in time



- Predictions up to 2 weeks ahead look good
- But can this be used to extract the epidemic?

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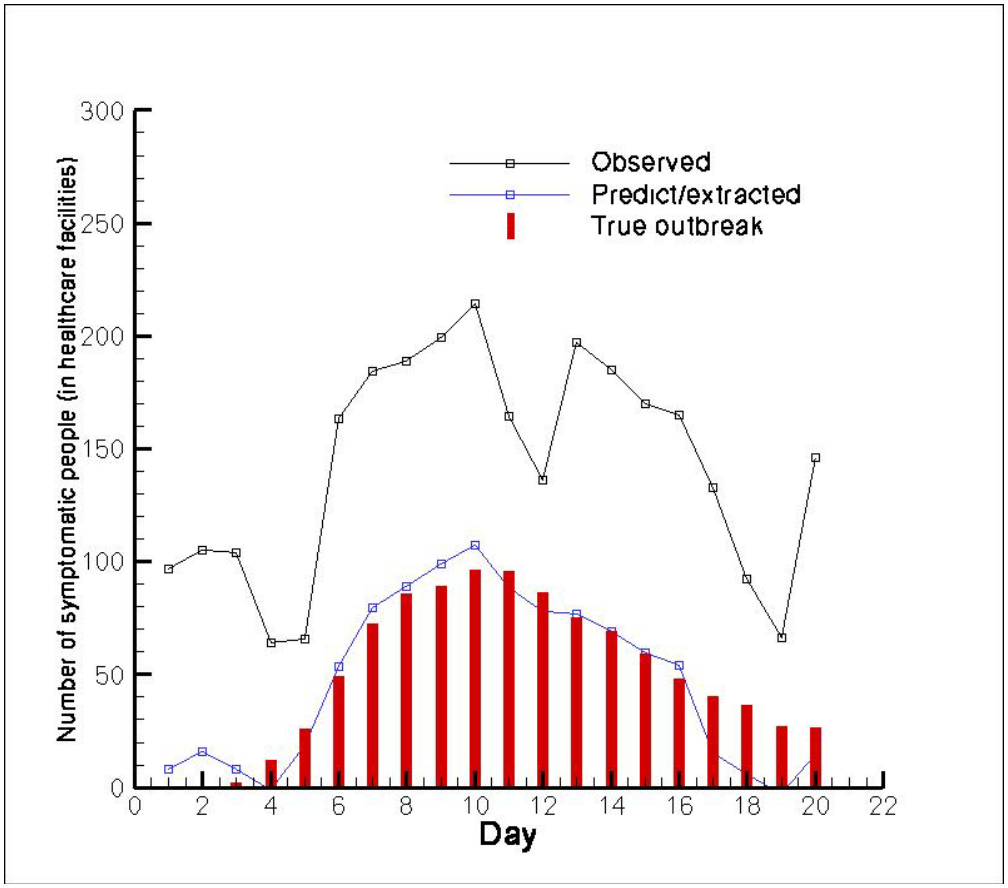
Extraction of the Epidemic Cont.

- Plot the difference between observations and predictions by frozen background model
- Estimate of the anthrax outbreak
  - Pretty good for 15 days
- However, it is a partial estimate
  - Extends only to the number of days of observations
- Can the partial anthrax outbreak be used for characterizing the attack?



Day 0 is day of release

Day 5 is day of detection

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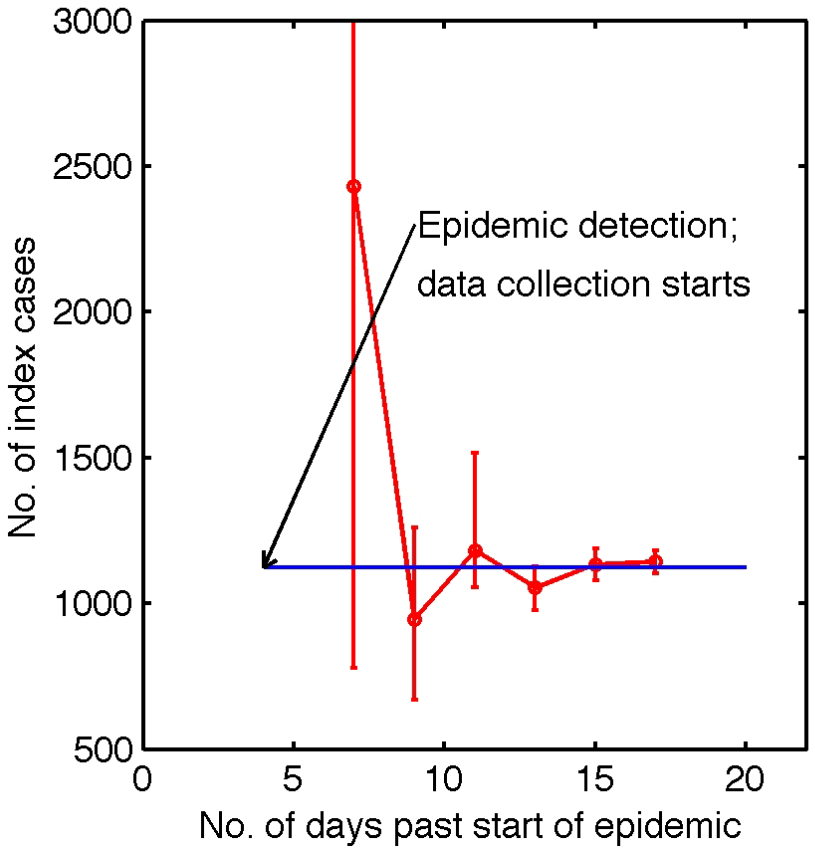
Characterization of the Anthrax Epidemic

- **Characterization:**
  - **Estimation of the number of index cases, time of release, an average dose, and some parameters of the visit-delay model**
- **Hypothesis:**
  - **An anthrax incubation period model + a visit delay model can reproduce the epidemic curve**
    - **The quantities of interest are all parameters/inputs into this epidemic model**
  - **So given a partial epidemic curve, fitting an anthrax model should reveal the necessary model parameters**
- **Questions:**
  - **How much data is needed to estimate these parameters?**
    - **i.e., is less than 15 days of (good, normal background extracted) data sufficient?**
  - **What is the level of uncertainty in parameter estimates, as a function of (quantity of) data?**

Bayesian Techniques to Solve the Problem

- The estimation is posed as a Bayesian inverse problem
  - Predicated on the extracted outbreak data
- Allows one to use bounds / prior beliefs regarding the value of the parameters
  - We assumed that index cases ranged between 100-10,000
- Solved using an adaptive Markov chain Monte Carlo sampler
  - All parameters estimated as probability density functions (PDF)
  - Used autocorrelation analysis to determine “convergence” of the Markov chain

Estimates of the Number of Index Cases



Number of index cases bounded in 7 days;

Bounded to 2250 people out of original population of 3 Million;

Accurate to 20% after 9 days, post detection.

Incubation period is 3-4 days so will not get earlier than that.

- Estimates of the number of index cases (in red).
- True figure in blue

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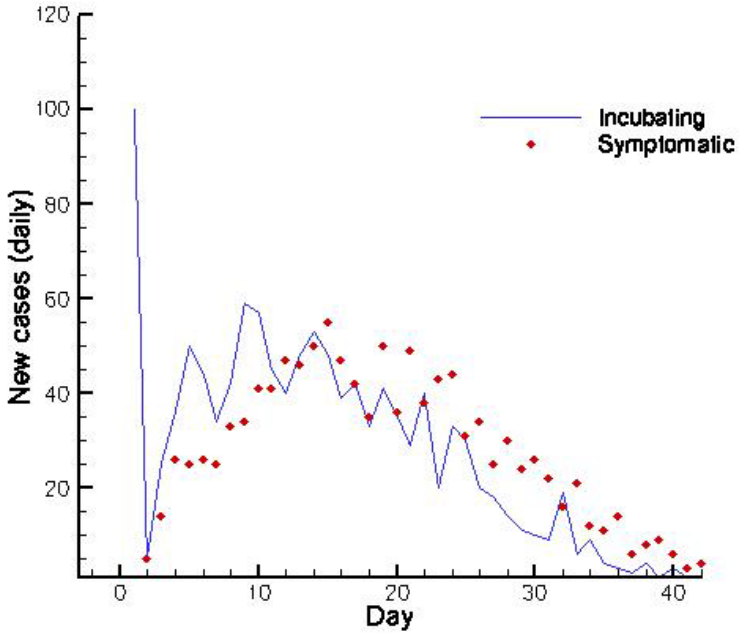
Application to a Communicable Disease

- The technique can be applied to a communicable disease
  - Need to estimate infection rate (along with “usual” parameters)
- Assumptions for communicable diseases model
  - The infection rate rises & then falls smoothly in time
  - Index cases are a small fraction of the total number of victims
- A lightweight model can be created and fitted to data
  - The model of epidemic evolution is statistical (not AB)
  - Is used with MCMC, as before
  - Allows inferences to be drawn as PDFs
- Demonstrate with synthetic data
  - Simulate a plague epidemic using an AB model

A Communicable Disease Example

- The simulated plague epidemic
  - Includes visit-delay
  - Incubation is NOT dose dependent
- 100 index cases
  - Epidemic dies out in 40 days
  - 1500 victims, total
- Aim:
  - Estimate the total size of the epidemic
  - Also, the infection rate curve
  - Compare with the “true” figures from the simulation



- Red points: People turning symptomatic, daily (observed)
- Blue line: people being infected, daily (unobservable)

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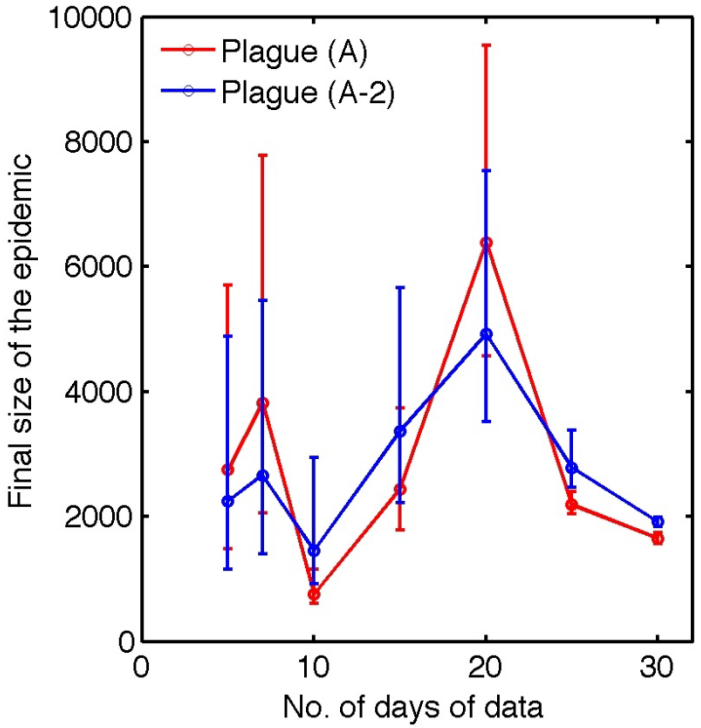
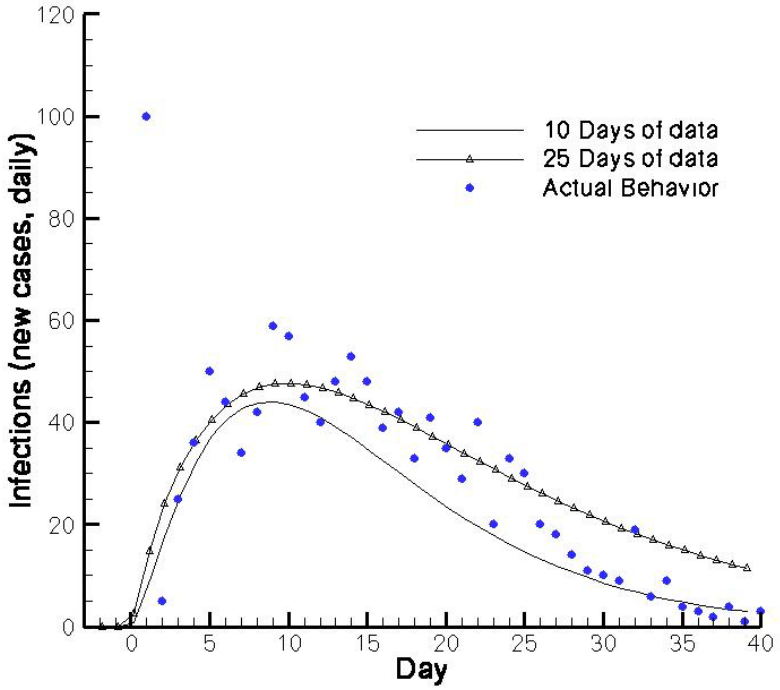
Estimation of the Final Epidemic Size



Final size of the epidemic (true figure = 1500)



Infection rate

- **The estimate improves (shorter error bars) with time**
- **Easier for large outbreaks**

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Conclusions

- Techniques appear promising to construct and integrate automated detect-and-characterize technique for epidemics
  - Working off biosurveillance data
  - Provides information on the particular/ongoing outbreak
- Potential use – in crisis management and planning, resource allocation
  - Parameter estimation capability ideal for providing the input parameters into an agent-based model
    - Index Cases, Time of Infection, infection rate
- Non-communicable diseases are easier than communicable ones
  - Small anthrax can be characterized well with 7-10 days of data, post-detection; plague takes longer
  - Large attacks are very easy