



Ross: A Networked-Epidemiology WebApp

August 25, 2014

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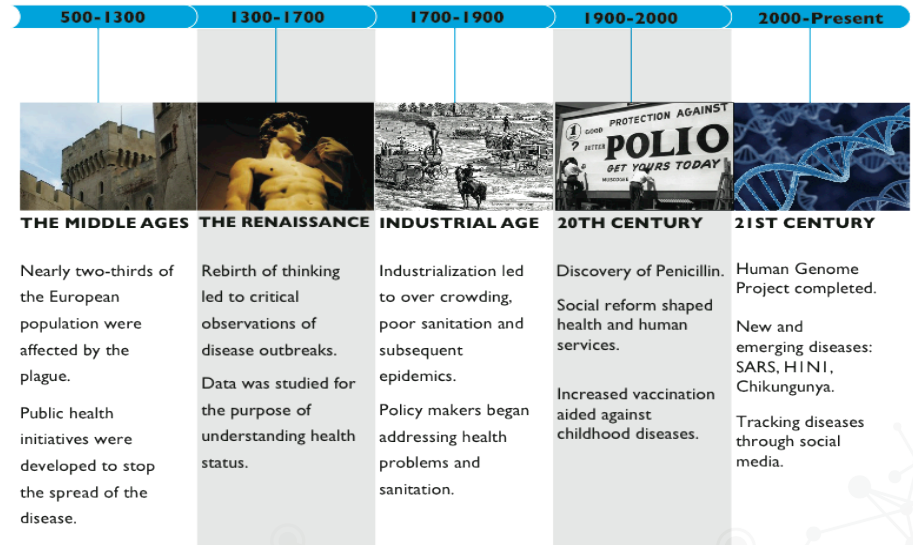
*Network Dynamics and Simulation Science Laboratory, VBI &
Dept. of Computer Science
Virginia Tech*



Epidemics and epidemiology in history

- Good news: Pandemic of 1918 lethality is currently unlikely
Governments better prepared and coordinated : e.g. SARS epidemic
But ..
- Planning & response to even a moderate outbreak is challenging: inadequate vaccines/anti-virals, unknown efficacy, hard logistics issues
- Modern trends complicate planning: increased travel, immuno-compromised populations, increased urbanization

HISTORY OF INFECTIOUS DISEASES

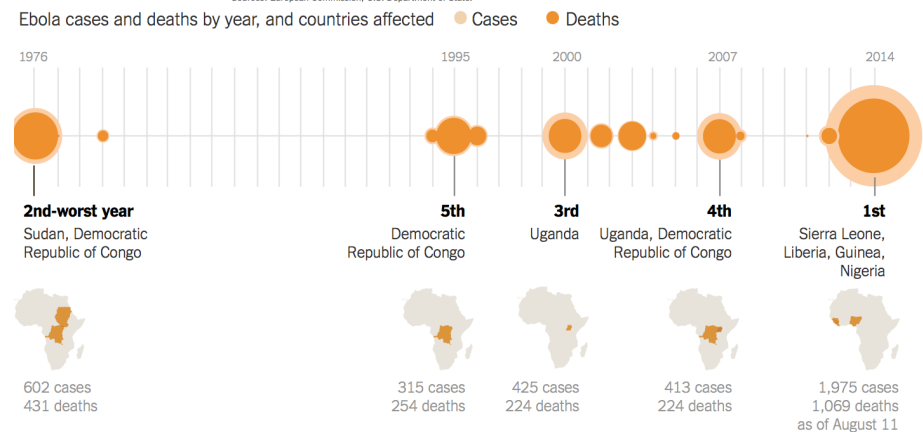


Need for modeling environments to support epidemiologists



Ebola outbreak in Africa

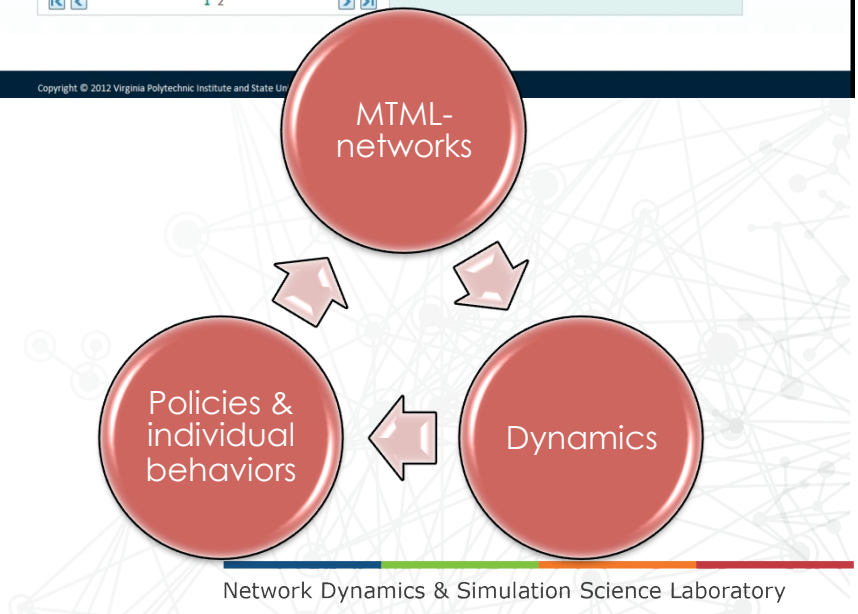
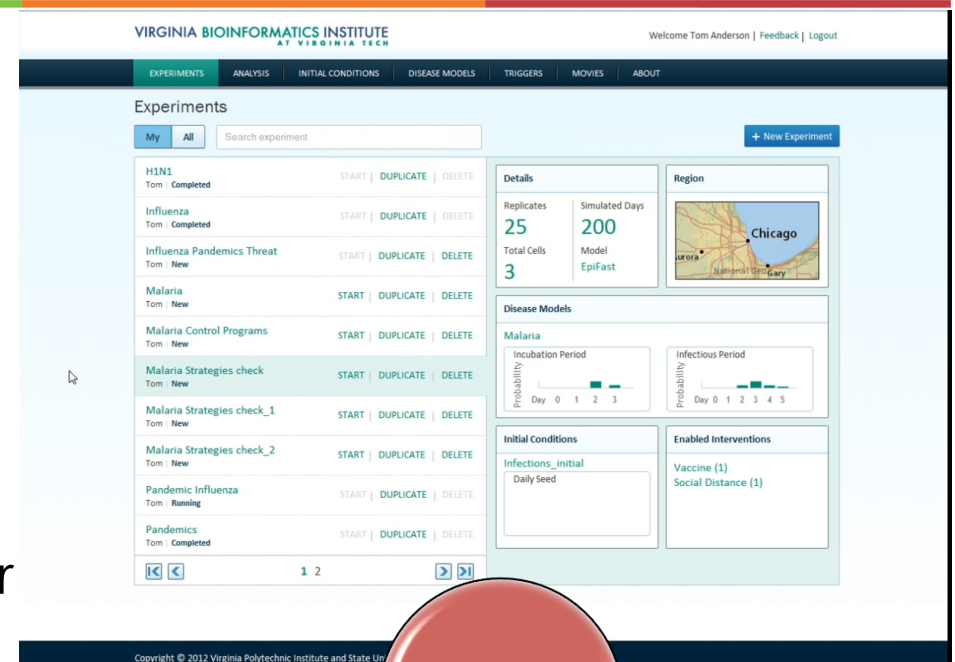
- Largest Ebola outbreak yet: 3 countries; 2000 cases; 1000 deaths.
- Beautifully done NY Times webpage: <http://www.nytimes.com/interactive/2014/07/31/world/africa/ebola-virus-outbreak-qa.html>
- Questions:
 - How many people have been infected?
 - Where is the outbreak?
 - How did it start; tracing the first few cases.
 - Chances of getting Ebola in the US?
 - How does this compare to past outbreaks?
 - How contagious is the virus?
 - Why is Ebola so difficult to contain?
 - How does the disease progress?
 - How is the disease treated?
 - Where does the disease come from?





What is Ross

- Ross (Interface to Synthetic Information Systems) is a web based tool to support real-time epidemic science.
 - Fineberg and Harvey, Science 2009.
- *Philosophy*: Sophisticated modeling environments should also be easy to by subject matter experts.
 - SMEs have no interest in becoming computer scientists !





Ross supports real-time epidemic science

EDITORIAL

- Modeling 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
- Modeling 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.iom.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).



Downloaded from www.sciencemag.org on October 7, 2009

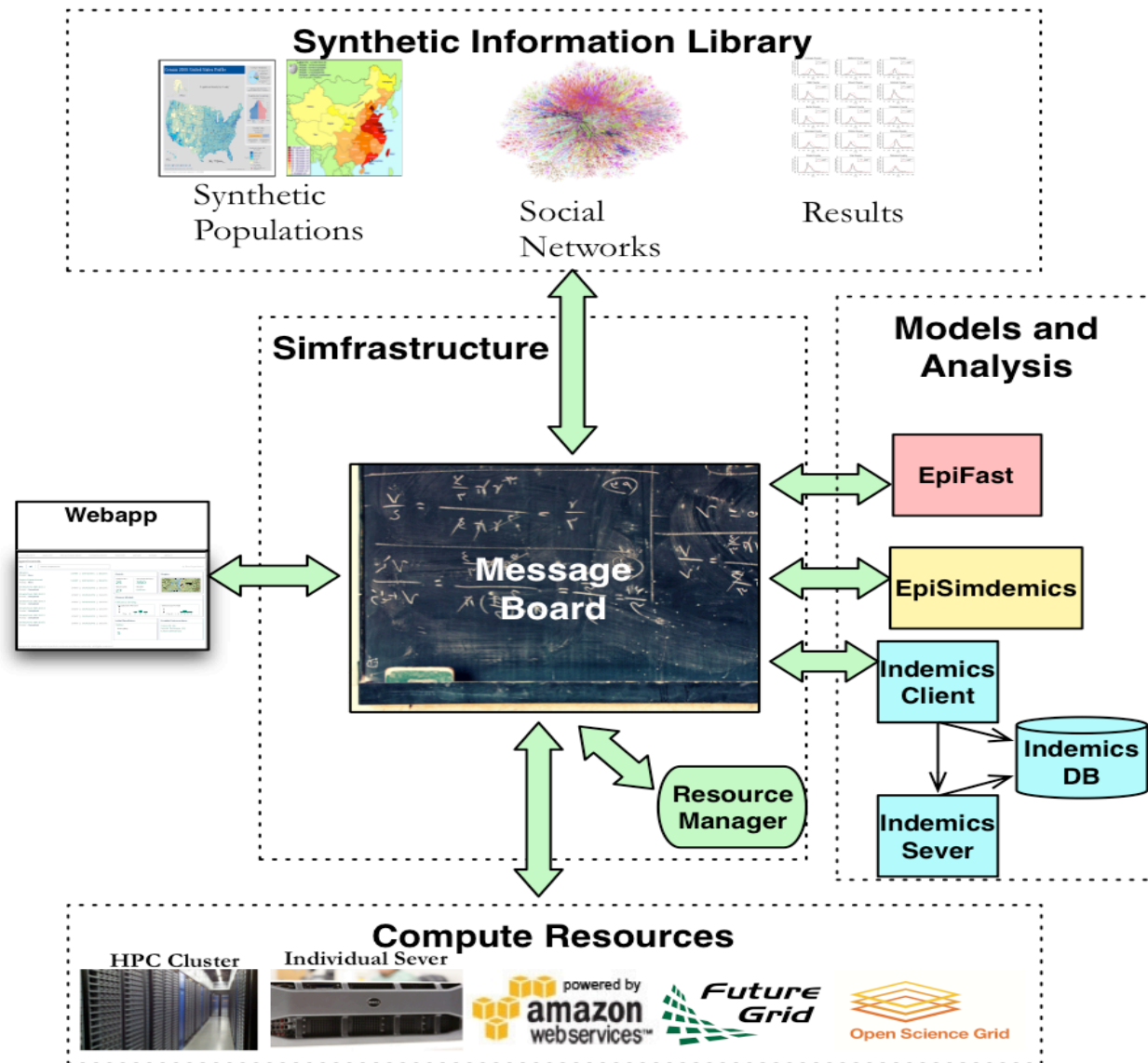


Ross Features

- Design, execute, analyze multi replicate, multi cell epidemiology experiments
- Specify social network, disease models, multiple parameterized interventions
- Real-world interventions:
 - Pharmaceuticals (e.g., Vaccination, Antivirals)
 - Work/School closure
 - Sequestration
 - Can be applied to specific subpopulations (school age children, critical workers)
 - Dynamic triggers (e.g., % infected children for school closure)
- Interactive Analysis
 - Automatic ordering of interventions by effect size



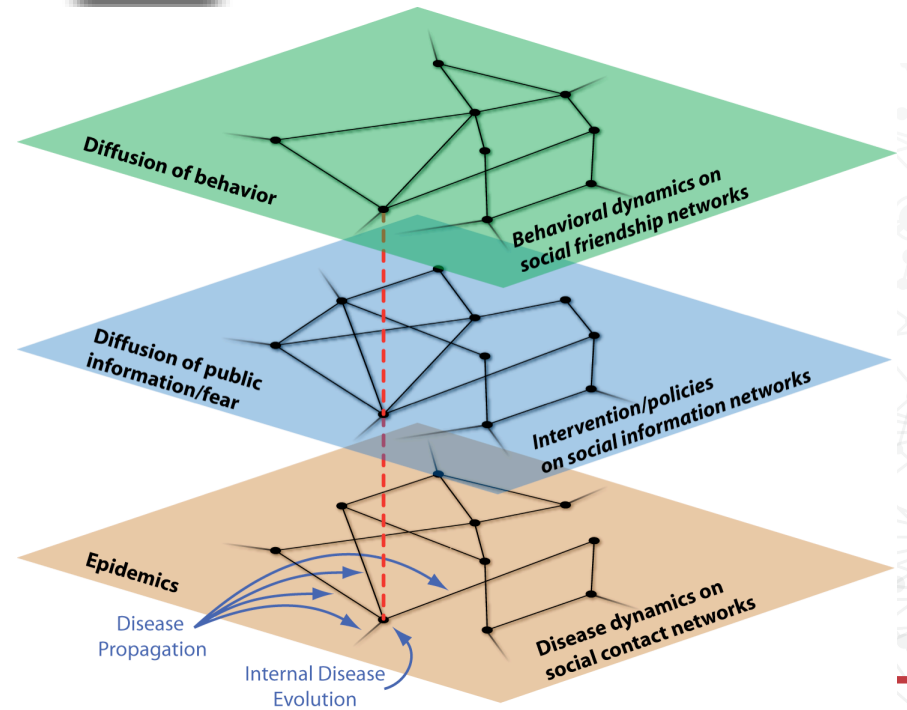
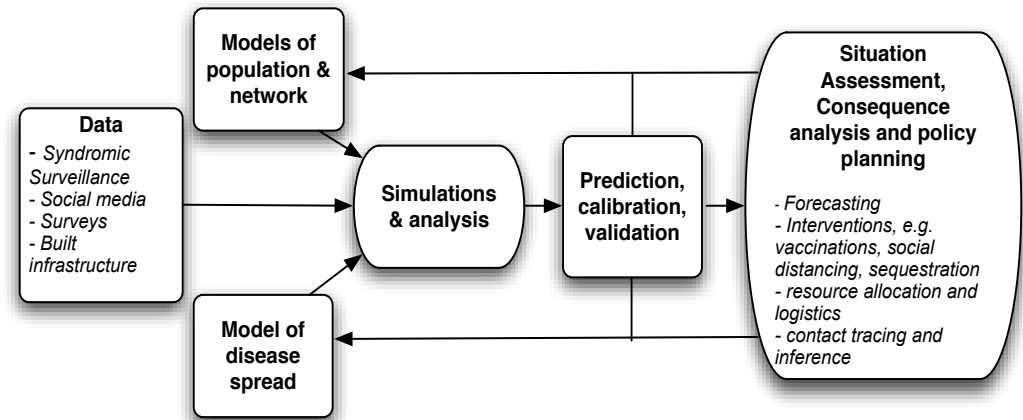
Ross Architecture





Ross supports networked epidemiology

- Supports complex experiments pertaining to epidemic dynamics, control and optimization over realistic but synthetic national scale social contact networks
- Supports multi-theory multi-network representations of the complex system – co-evolution of networks, epidemics, behavior and policies can be undertaken

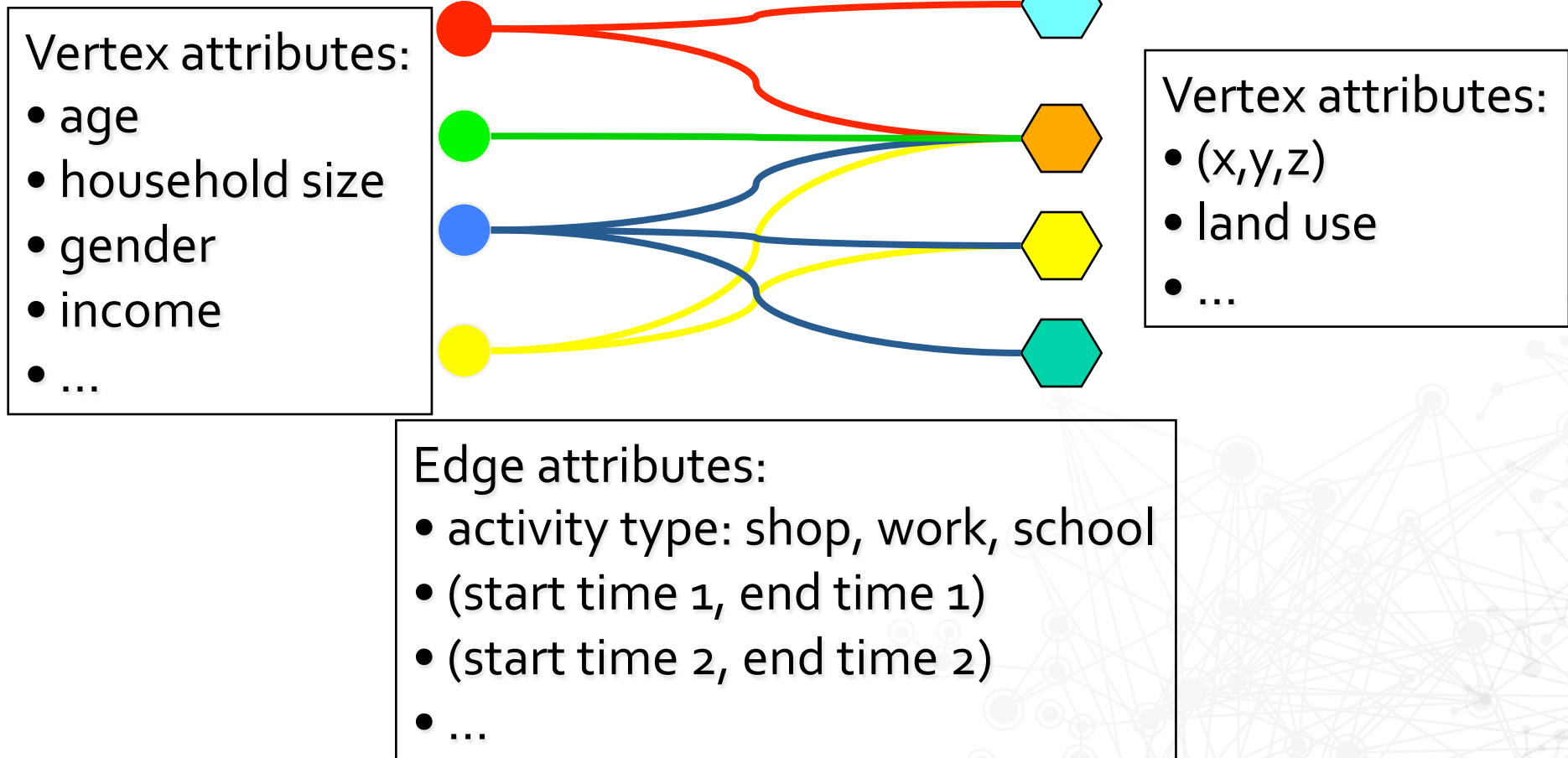




Supports analysis over dynamic social contact networks

People (8 million)

Locations (1 million)





Supports large and realistic social contact networks

Input files

- Population data
- Scenario
- Disease model
- Runtime configuration

Output files

- Disease
- Dendrogram
- Social net

Population data selected for study

data	visits	people	locations
US	1,541,367,574	280,397,680	71,705,723
CA	183,858,275	33,588,339	7,178,611
NY	98,350,857	17,910,467	4,719,921
MI	52,534,554	9,541,140	2,490,068
NC	47,130,620	8,541,564	2,289,167
IA	15,280,731	2,766,716	748,239
AR	14,803,256	2,685,280	739,507
WY	2,756,411	499,514	144,369

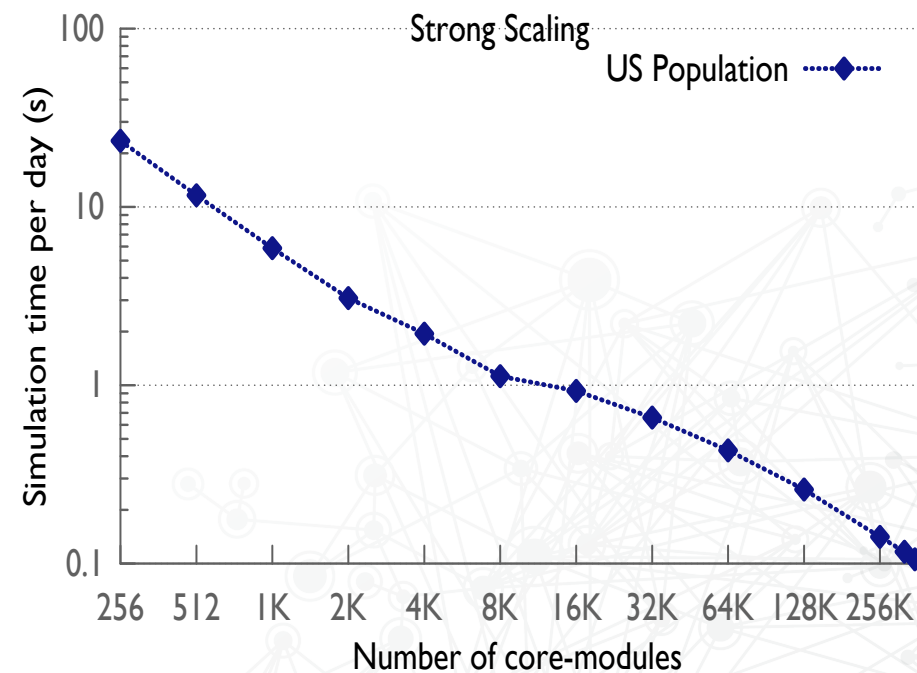
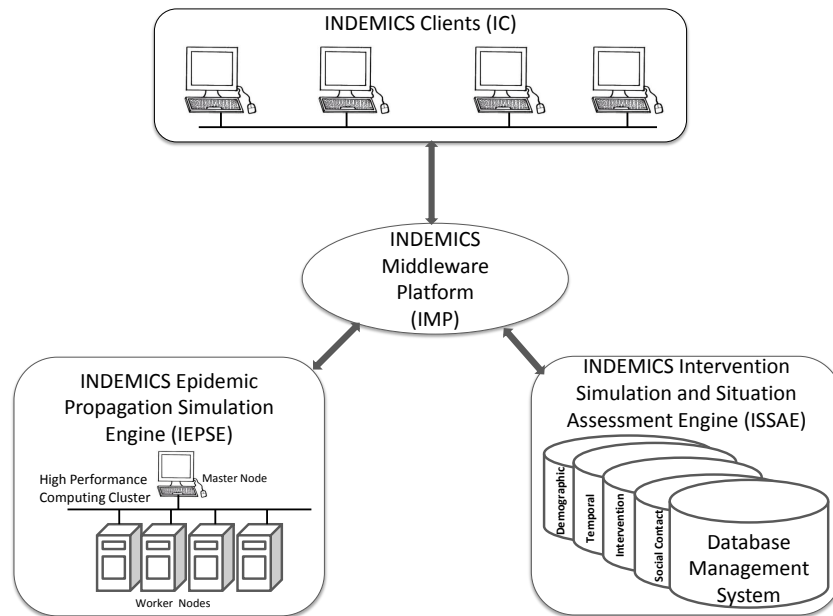
Table : Population data³ based on various sources including 2009 American Community Survey. US includes 48 contiguous states and DC.

³ C. Barrett et al., "Generation and Analysis of Large Synthetic Social Contact Networks," WSC09.



Ross supports HPC simulation engines

- *EpiSimdemics*: highly scalable HPC simulation: scales gracefully over 350K cores
- *Epifast*: a consumer-producer style simulation
- *Indemics*: database driven interactive simulation



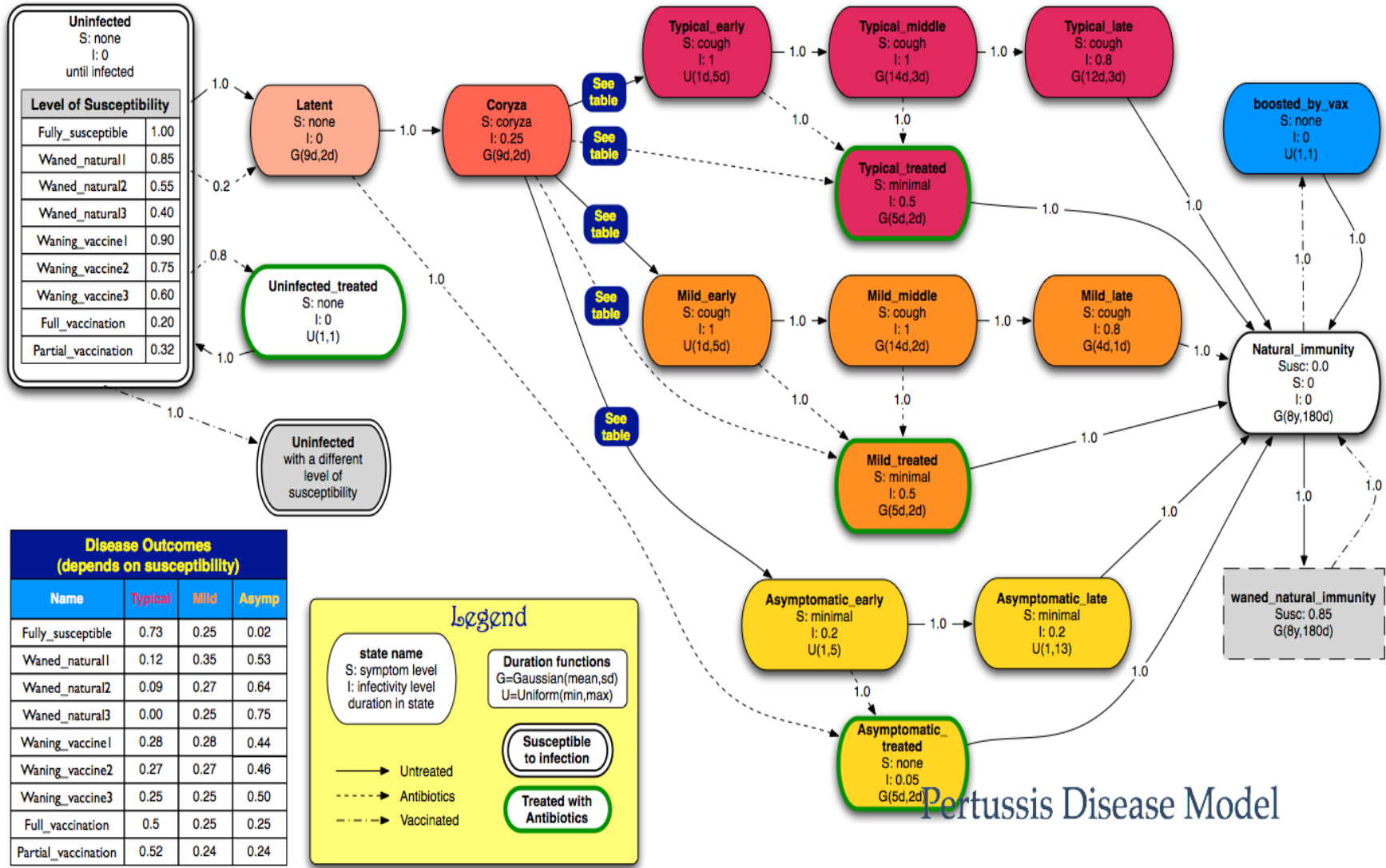


Supports complex interventions

component	specification	example
trigger	scheduled threshold	winter break Dec. 21–Jan. 3 prevalence > 0.05
subpopulation	demographic geographic social health combination of above	seniors people in Fairfax county, Virginia critical workers diagnosed (flu) people diagnosed seniors in Fairfax county
action	vaccination antiviral school closure work closure isolation combination of above	effects: enhance immunity reduce symptoms or infection probability remove school activities and in-school contacts remove work activities and at-work contacts remove all contacts combined effects



Supports detailed disease representation





Bigdata challenge: Example of a 20 Cell, 20 replicate design

Area	Population (Nodes in Millions)	Interactions (Edges in Millions)	Input Data (GB)	Output Data (GB)	Compute time days (2000 cores)	Compute Time, Days (300K cores)
West Coast	43	2500	35	3	6	.1
East Coast	75	3750	60	5	10	.2
Entire USA	280	14,000	225	20	43	.8
North America	518	29,000	416	37	80	1.6
Global Population	6500	325,000	5223	464	1000	20



Complete analyst workflow support

Hypothesize

Experiments

My All Search experiment

- Influenza Like Illnesses (Mary | Completed) [START] [DUPLICATE] [DELETE]
- Influenza Pandemics Threat (Tom | New) [START] [DUPLICATE] [DELETE]
- Liver Cancer (Mary | New) [START] [DUPLICATE] [DELETE]
- Malaria Control Programs (Tom | New) [START] [DUPLICATE] [DELETE]
- Malaria Strategies check (Tom | New) [START] [DUPLICATE] [DELETE]
- Malaria Strategies check_1 (Tom | New) [START] [DUPLICATE] [DELETE]
- Malaria Strategies check_2 (Tom | New) [START] [DUPLICATE] [DELETE]
- Outbreaks - zoonoses (Linda | New) [START] [DUPLICATE] [DELETE]
- Pandemic Influenza (Mary | Completed) [START] [DUPLICATE] [DELETE]
- Pandemic Influenza

Details

Replicates: 25 Simulated Days: 200

Total Cells: 1 Model: EpiFast

Region

Disease Models

AL_25 Moderate flu

Incubation Period: Probability Day 0 1 2 3

Infectious Period: Probability Day 0 1 2 3 4 5 6

Enabled Interventions

- Vaccine (1)
- Close Work (1)
- Close School (1)
- Antiviral Treatment (2)
- Antiviral Prophylaxis (1)

Initial Conditions

S_FIRST_DAY

OnDay0: 5

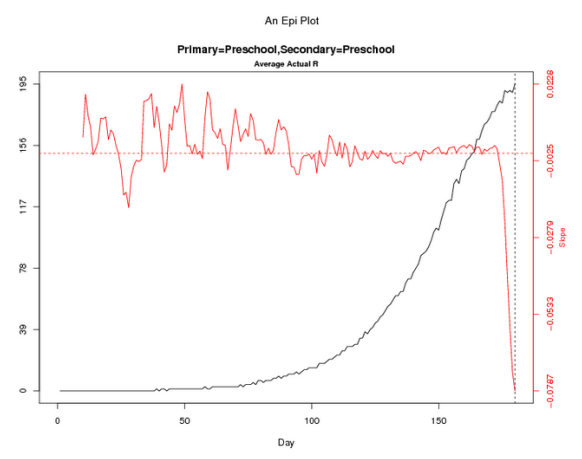
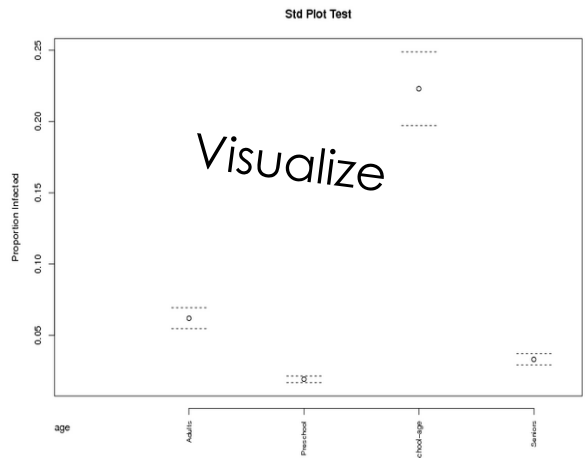
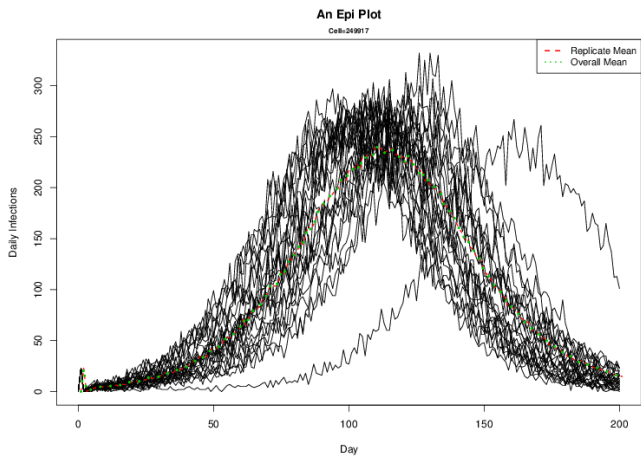
Model

Region: Boston

Search region

- Boston
- Chicago
- Dallas
- Detroit
- Los Angeles
- Los Angeles w/ military
- Miami
- Montgomery
- New York City
- Seattle
- Seattle w/ military
- Washington

Predict, Decide





Experiments dashboard

EXPERIMENTS | ANALYSIS | INITIAL CONDITIONS | DISEASE MODELS | TRIGGERS | MOVIES | ABOUT

Experiments

My All Search experiment

+ New Experiment

Filter

Search

Execution Status

History of Sessions

Endemic H1N1 Mary New	START DUPLICATE DELETE
Cholera Interventions Mary Completed	START DUPLICATE DELETE
Cholera Outbreak Mary Completed	START DUPLICATE DELETE
H1N1 Vaccine, Boston John Failed	START DUPLICATE DELETE
H1N1 Vaccine, Chicago John New	START DUPLICATE DELETE
H1N1 Vaccine, Seattle John New	START DUPLICATE DELETE
H1N1 Vaccine, Washington John New	START DUPLICATE DELETE
HIV Related Gingivitis Mary New	START DUPLICATE DELETE
Influenza Epidemics 1 Mary New	START DUPLICATE DELETE
Influenza Epidemics 2 Mary New	START DUPLICATE DELETE

Details

Replicates	25	Simulated Days	200
Total Cells	72	Model	EpiFast

Region

Disease Models

H1N1 - Catastrophic

Incubation Period	Infectious Period

Initial Conditions

Init 7

OnDay0

7

Enabled Interventions

- Vaccine (1)
- Close Work (1)
- Close School (1)
- Antiviral Treatment (2)
- Antiviral Prophylaxis (1)



Disease models

Ability to model wide range of Disease Progression

The screenshot shows the 'Experiments' dashboard of the Virginia Bioinformatics Institute. It features a table of experiments with columns for name, status, and actions. A search bar is at the top. On the right, there are summary cards for 'Details' (Replicates: 25, Total Cells: 36, Simulated Days: 200), 'Region' (map of Boston area), 'Disease Models' (Incubation and Infectious period graphs), 'Initial Conditions' (Init: 7, OnDay: 0), and 'Enabled Interventions' (Vaccine, Social Distance, Close Work, Close School, Antiviral Treatment, Antiviral Prophylaxis).

This section shows a detailed view of the 'Endemic H1N1' experiment. It includes a sidebar with a list of models, a main details panel, and two graphs showing the probability of infection over time for different days.

Model List:

- H1N1 - Catastrophic
- H1N1.catastrophic.Elaine
- H1N1.mild.Elaine
- H1N1.moderate.Elaine
- H1N1.strong.Elaine
- Hepatitis
- Influenza Strong flu
- Malaria
- Mild flu

Details Panel:

- Name: H1N1 - Catastrophic
- Owner: sample
- Transmissibility: 0.000083
- Description: H1N1 catastrophic influenza

Graph 1: Incubation period

Days	Probability
0	0.200
1	0.450
2	0.350

Graph 2: Infectious period

Days	Probability
0	0.010
1	0.660
2	0.660
3	0.330
4	0.010



Interventions

EXPERIMENTS

ANALYSIS

INITIAL CONDITIONS

DISEASE MODELS

TRIGGERS

MOVIES

ABOUT

[Back](#)

Endemic H1N1

Enabled Interventions



Summary



Vaccinate



Social Distance



Close Work



Close School



Antiviral Treatment



Antiviral Prophylaxis

Your Interventions

Vaccine

Vaccine 1 : School-age (796389)

Close Work

Close Work 1 : Adults (2570050)

Close School

Close School 1 : School-age (796389)

Antiviral Treatment

Antiviral Treatment 1 : Adults (2570050)

Antiviral Treatment 2 : All (4149279), School-age (796389),

Adults (2570050)

Antiviral Prophylaxis

Antiviral Prophylaxis 1 : Seniors (503723), Adults (2570050),

Preschool (279117), School-age (796389)



Analysis

Back

Cholera Epicurve - Results

Download

Graph

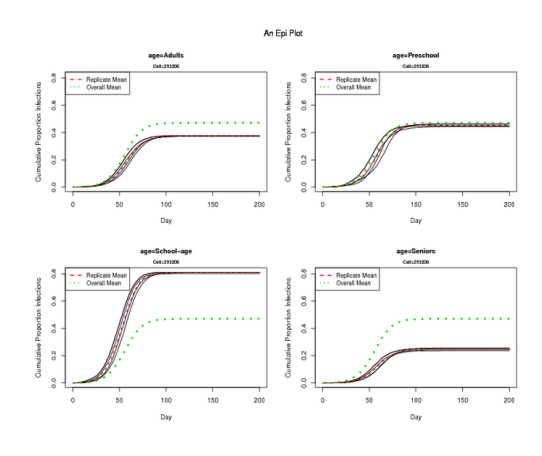
Intervention Summary

Means Table

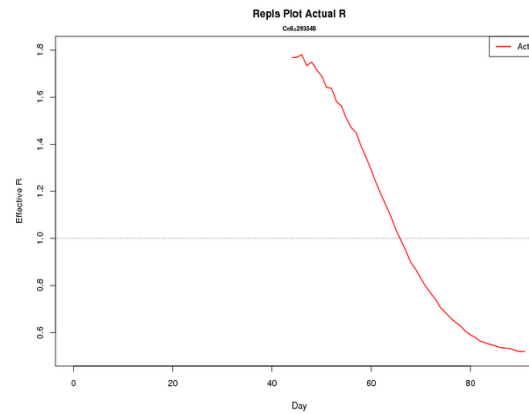
Daily Mean Infection

Preview and also Download Tables and Graphs to use in other applications

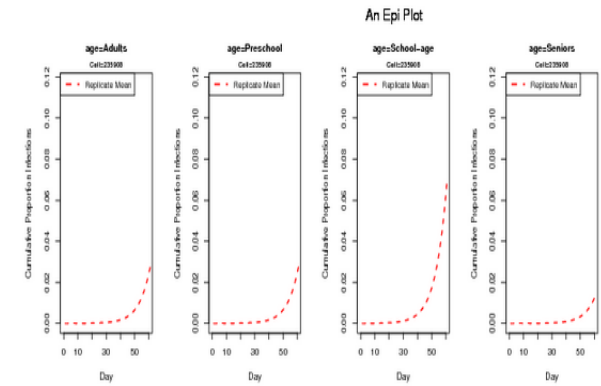
Age-wise Epicurves



Reproductive numbers



TIGS Analysis Support



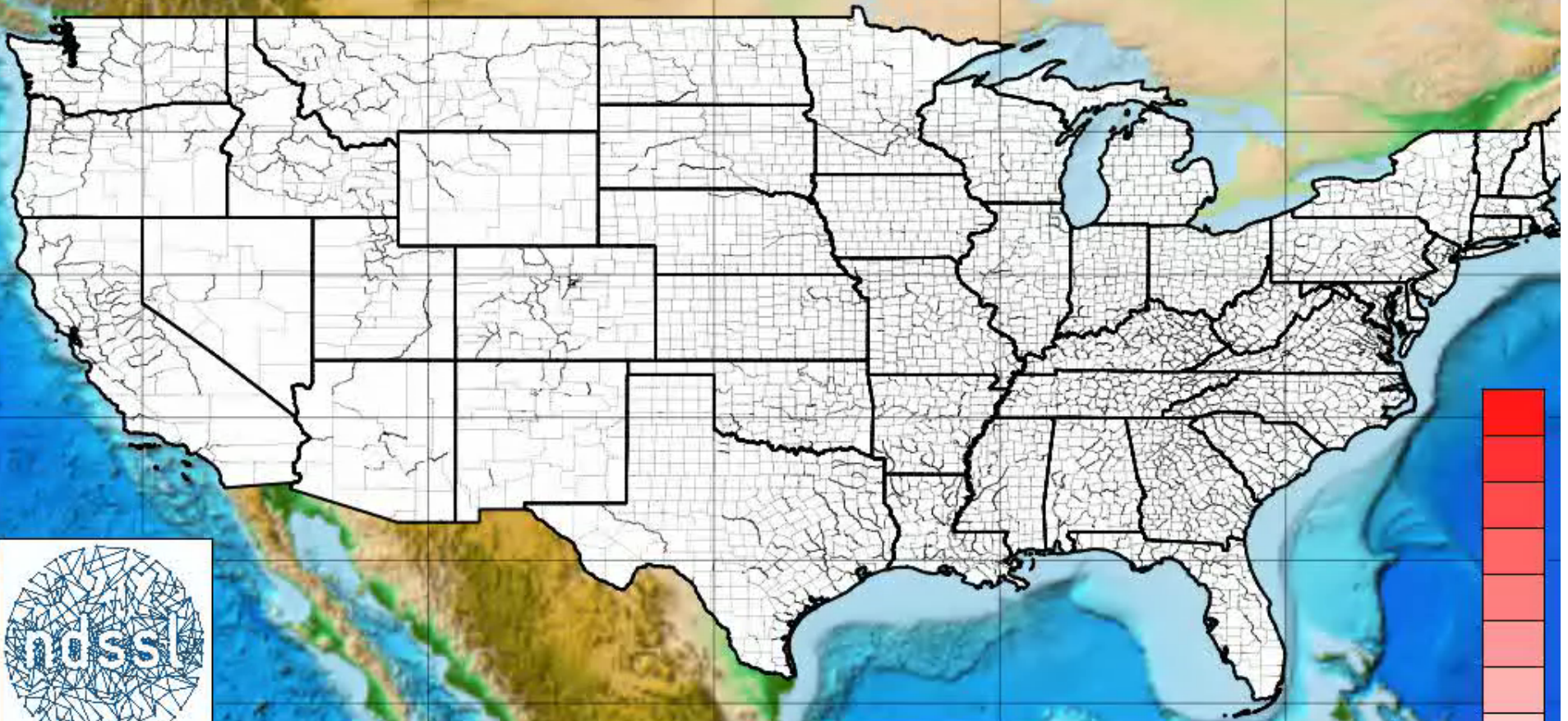


Selected Case Studies

- Pandemic Influenza Planning – Fall 2006
 - How can we prepare for a likely influenza pandemic?
- Emergence of H1N1 Influenza – Spring - Fall 2009
 - What are the characteristics of this influenza strain and their likely impact on US populations?
- Optimizing Household Response to Epidemics – Spring 2011
 - Do behaviors within households, while harder to simulate, have a significant impact on the course of an epidemic?
- SLE: Adenovirus Pandemics Simulation and Analysis – August 2013
 - How can decision makers become familiar with the challenges and decisions they are likely to encounter during a national pandemic, mainly centered on the allocation of scarce resources?
- Emergence of Middle East Respiratory Syndrome – May 2014
 - We are exploring how simulation combined with a synthetic informatics analytic approach might shed light on what may be driving this outbreak.
- EBOLA – Ongoing

Day: 0
Number infected: 0

Spread of Adenovirus 12v across the US (scaled infection counts per day by county)



 **Virginia Tech**
Virginia Bioinformatics Institute

Outbreak seeded in Las Cruces, NM followed by Denver, CO and Visalia, CA. Disease is highly infectious but spreads slowly due to long incubation period. After 650 days of simulation without any mitigation strategies 43% of country has been infected.



Modeling

Case Studies

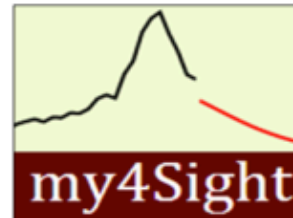
Press/Videos

Publications

Applications

About us

Welcome to the Network Dynamics & Simulation Science Laboratory applications page. In our pursuit of advanced research in synthetic information systems, we have developed a number of integrative applications that help to answer questions posed by scientists, policy makers, and planners involved with very large complex systems. Our tools and applications support real world decisions in areas that include public health, transportation, urban planning, communication, community resilience, and much more. From tabletop exercises to classroom lessons, the breadth of our applications reaches a diverse audience.



ndssl.vbi.vt.edu/apps





Demo: Ross V2.3

ISIS | VIRGINIA BIOINFORMATICS INSTITUTE
AT VIRGINIA TECH

Welcome Sample User | Feedback | Logout

EXPERIMENTS | ANALYSIS | INITIAL CONDITIONS | DISEASE MODELS | TRIGGERS | REAGENTS | MOVIES | ADMIN | ABOUT

Experiments

My All Search experiment + New Experiment

[321] Flu Failed 1 Cell Oct 07 2013, 07:33 Sample	RESTART VIEW ERRORS More Actions ▾
[62] H1N1 New 1 Cell Sep 30 2013, 09:46 Sample	START More Actions ▾
[245] Mild Flu Completed 1 Cell Oct 30 2013, 04:32 Sample	START More Actions ▾
[246] Yellow Fever Completed 1 Cell Oct 30 2013, 04:55 Sample	START More Actions ▾
[247] Influenza Completed 1 Cell Oct 30 2013, 04:58 Sample	START More Actions ▾
[248] Mild Flu Overseed 12 Cells Oct 30 2013, 05:02 Sample	START More Actions ▾
[249] Flu Overseed 4 Cells Oct 30 2013, 05:19 Sample	START More Actions ▾
[323] Yellow Fever New 12 Cells Oct 30 2013, 07:00 Sample	START More Actions ▾

1 2 3 4 ... 7

Details

Replicates: 1 Simulated Days: 1
Total Cells: 1 Model: EpiFast

Region

Disease Models

AI_25 Catastrophic Flu

Incubation Period: Probability vs Day (0-3)

Infectious Period: Probability vs Day (0-6)

Initial Conditions

30eachfor5
Daily Seed: Infected vs Day (0-5)

Enabled Interventions

Vaccine (1)
Social Distance (1)

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ndssl.vbi.vt.edu/apps/Ross