Computational epidemiology

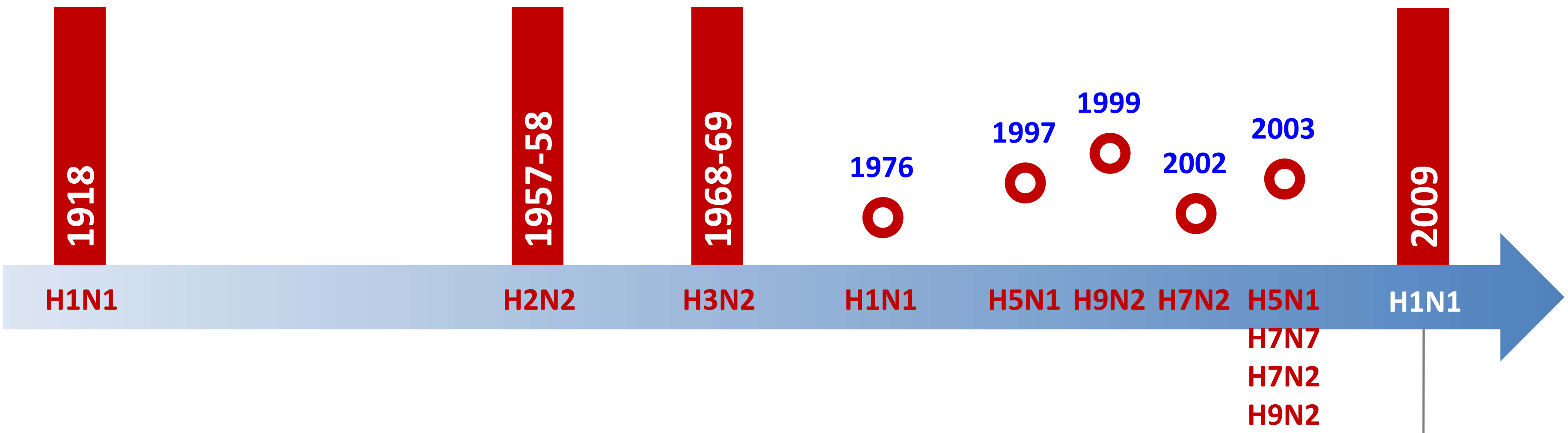
a new paradigm
in the fight
against infectious diseases

Vittoria Colizza

Computational Epidemiology Lab
ISI Foundation
Turin, ITALY

INSTITUTE
FOR SCIENTIFIC INTERCHANGE
FOUNDATION

pandemics



armory of weapons:

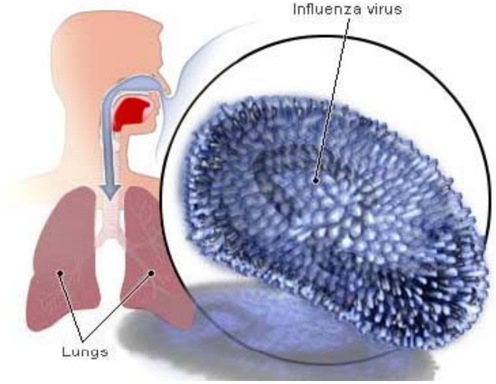
virology
gene sequencing
medicine
immunology
epidemiology
risk communication
social / information / computer sciences
modeling

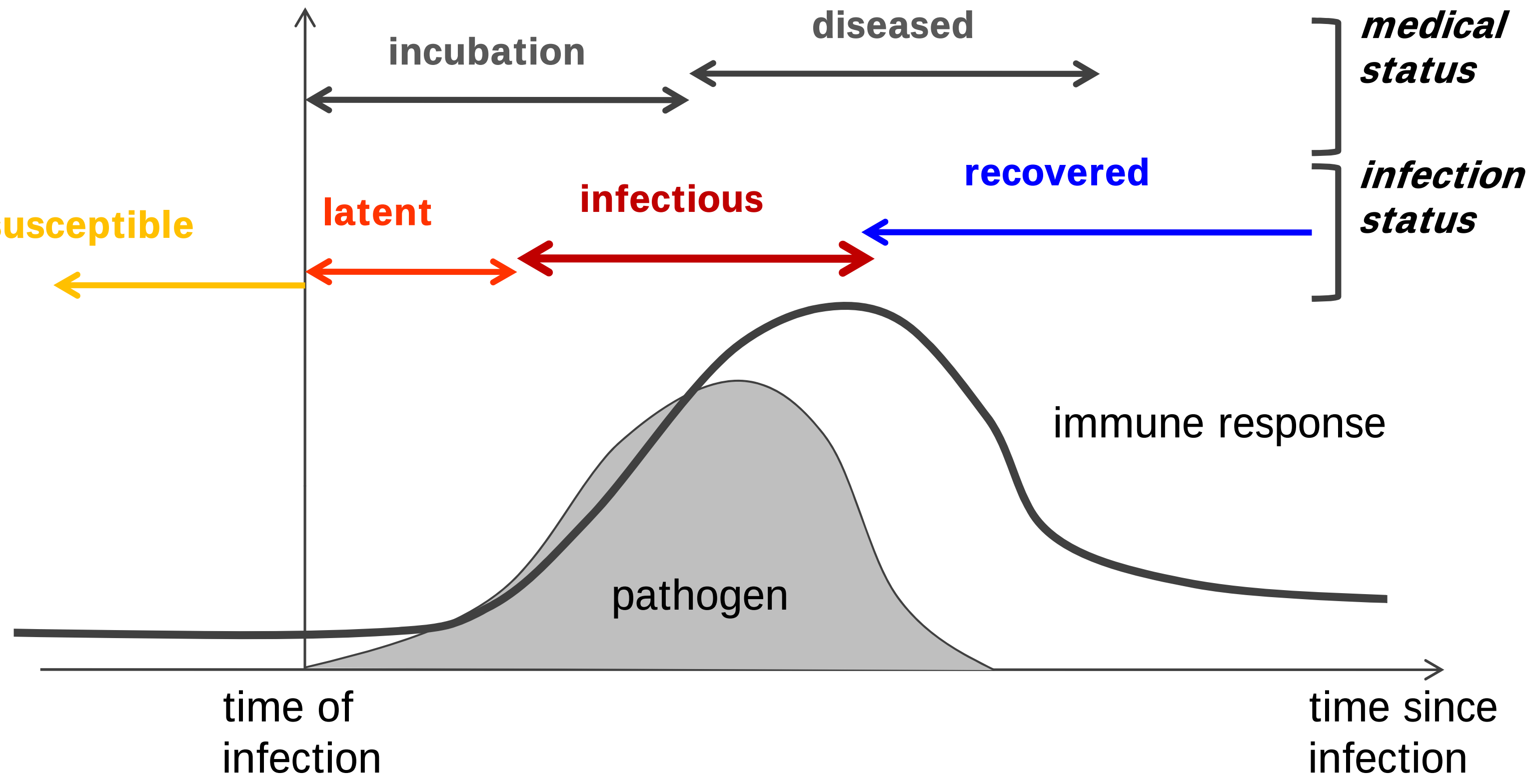
public health ←

Table 3.2 Notifiable infections in the United States (1984)

Acquired Immunodeficiency Syndrome (AIDS)
Amoebiasis
Anthrax
Aseptic meningitis
Botulism
Brucellosis
Chancroid
Cholera
Diphtheria
Encephalitis, primary
Encephalitis, post infectious
Gonorrhoea
Granuloma inguinale
Hepatitis, serum
Hepatitis, infectious
Hepatitis, unspecified
Leprosy
Leptospirosis
Lymphogranuloma venereum
Malaria
Measles
Meningococcal infections
Mumps
Pertussis
Plague
Poliomyelitis
Psittacosis
Rabies, animal
Rabies, human
Rheumatic fever, acute
Rubella
Rubella Congenital Syndrome
Salmonellosis
Shigellosis
Smallpox
Streptococcal sore throat and scarlet fever
Syphilis
Tetanus
Trichinosis
Tularemia
Typhoid fever
Typhus fever, flea borne
Varicella
Yellow fever

virus-host


Influenza virus
Lungs


incubation
diseased
medical status
susceptible
latent
infectious
recovered
infection status
immune response
pathogen
time of infection
time since infection

host-host

SocioPatterns.org

SPREADING THE FLU

Even a pandemic can have a silver lining. A flood of visitors to an Irish exhibition about e
has become a mother lode of data on the spread of disease.

On 17 April, the Science Gallery at Trinity College Dublin launched an exhib
INFECTIOUS. To give visitors a firsthand feel for "epidemic processes," everyon
radio-frequency identification tag. Tags are initially "uninfected" but can get "infe
proximity to "infected" staff or visitors. A computer tracks everyone, mapping the s
the infection.

The timing turned out to be propitious. Soon after the opening, swine flu panic hit. "We've had an amazing response," with more than 13,000 visitors so far, says gallery director Michael John Gorman. The data are flowing to computers in Italy, where epidemiologists at the Institute for Scientific Interchange Foundation in Turin are modeling epidemics. The experiment "does seem to address human-to-human contact at the most local level, which is the least well understood of organizational scales," says Oliver Pybus, an epidemiologist at the University of Oxford in the United Kingdom.

www.sciencemag.org SCIENCE VOL 324 22 M

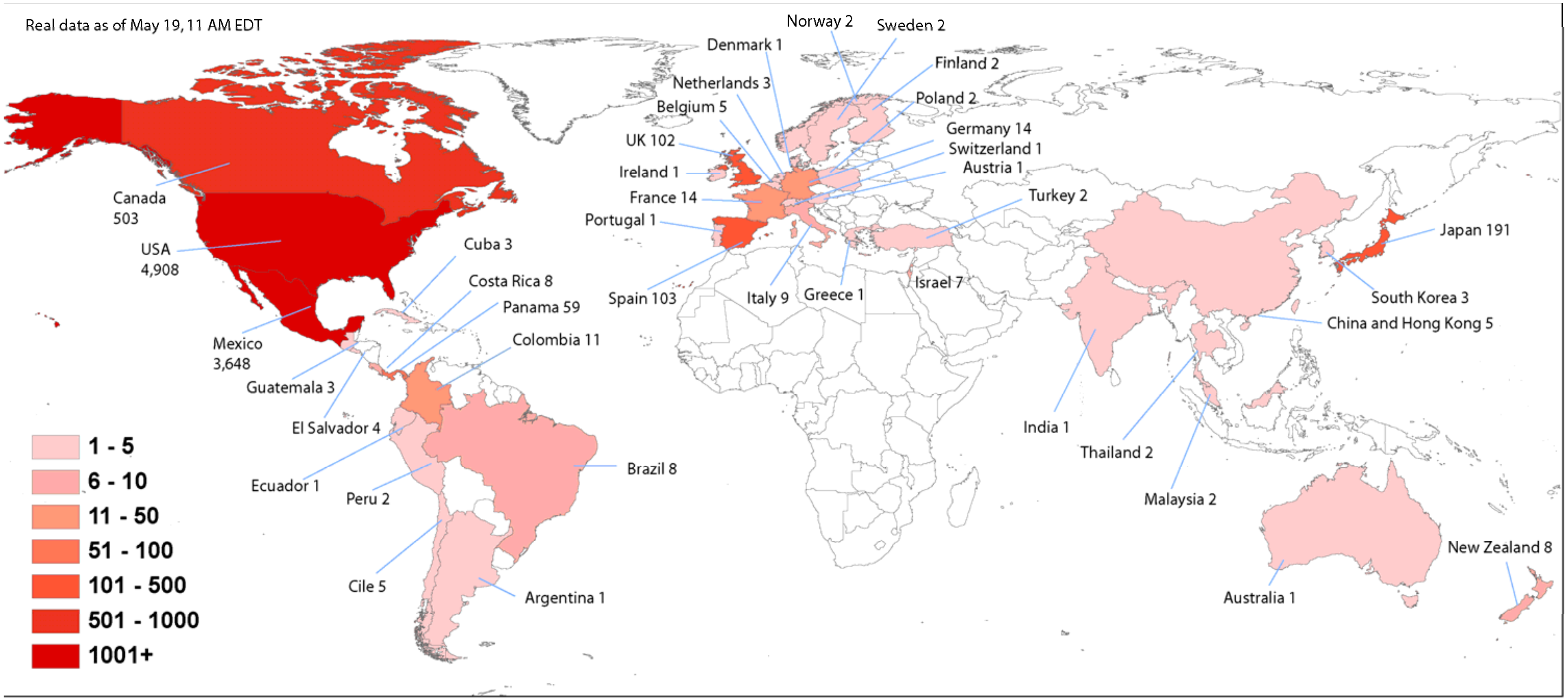
Published by AAAS

Science AAAS

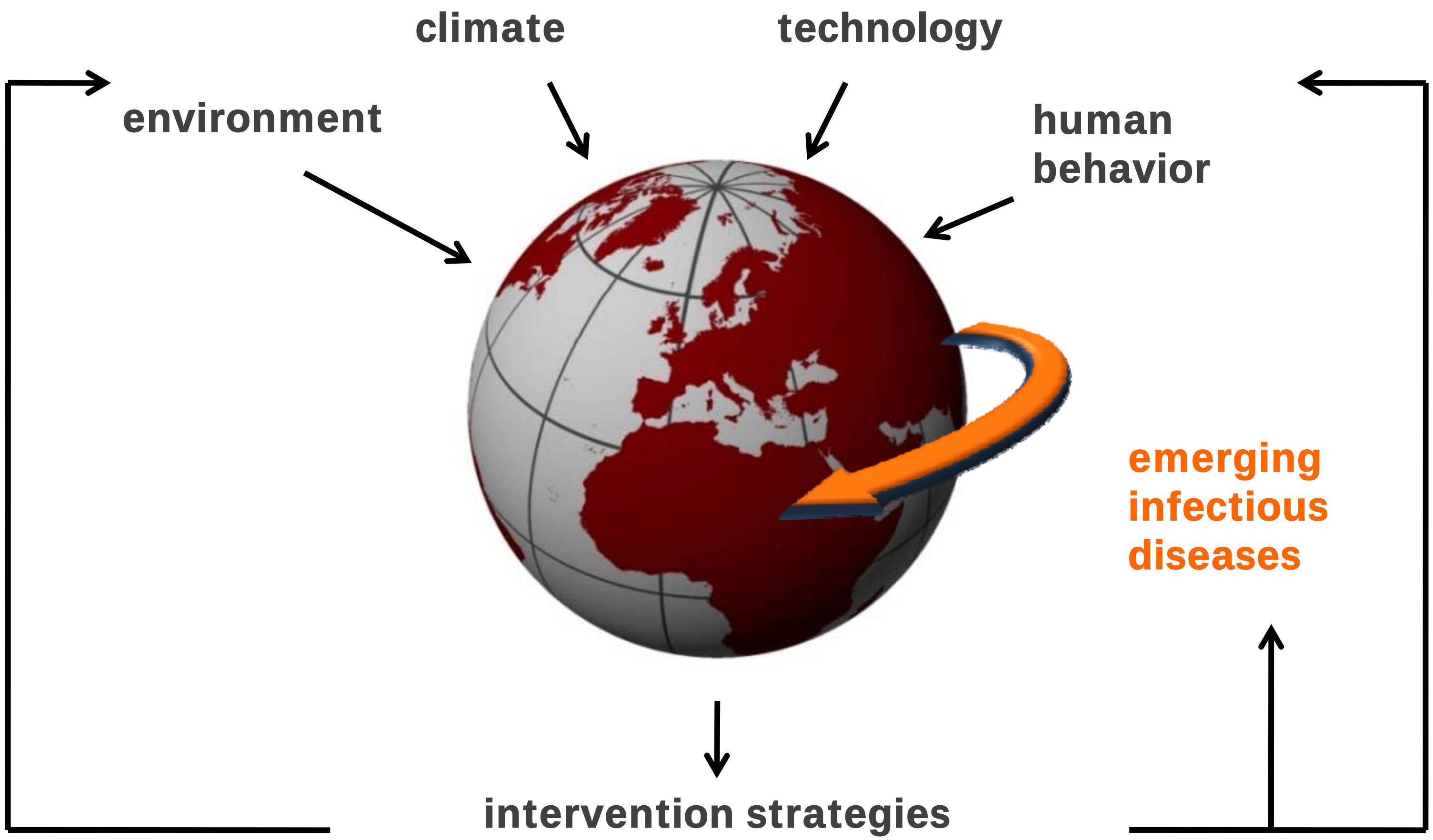
SCIENCE GALLERY

Cattuto et al. PLoS ONE (2010)

population & space



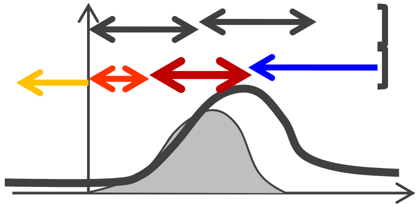
population, space & environment



multi-scale

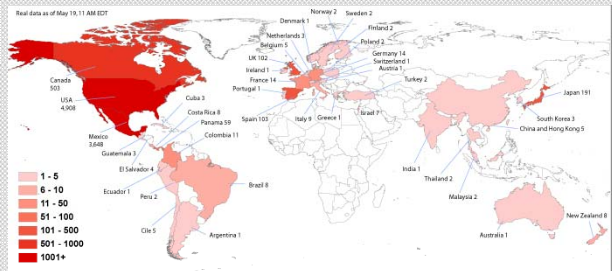
… …

virus-host interaction

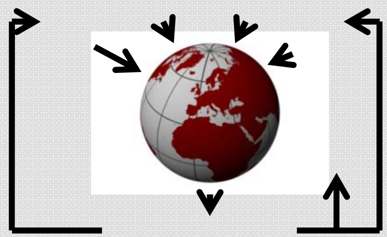


host-host interaction

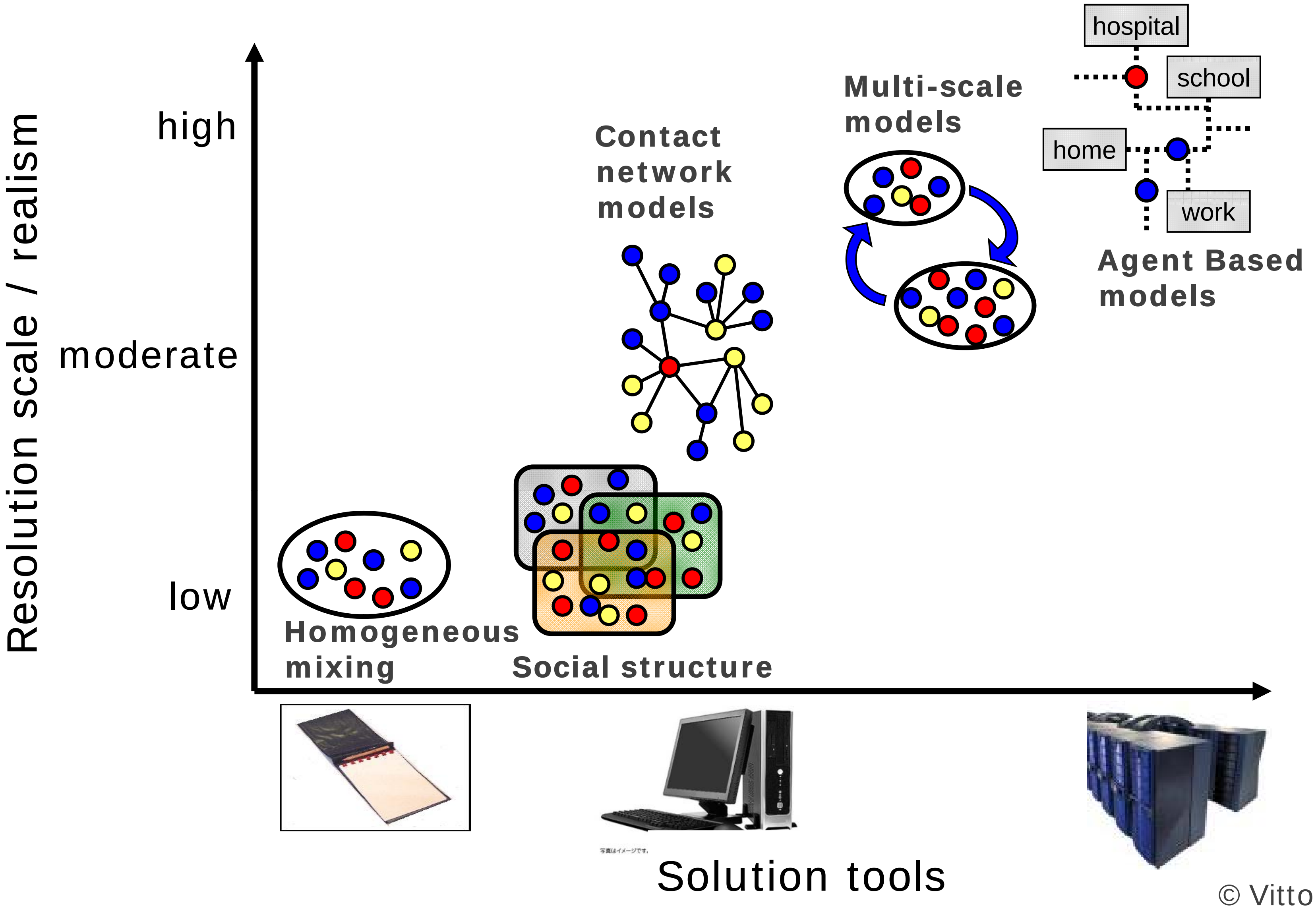
population & space



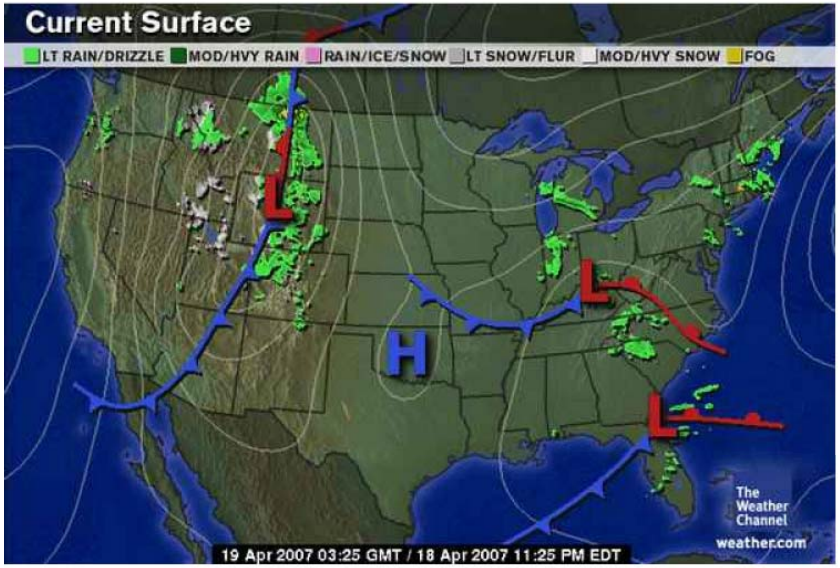
population, space & environment



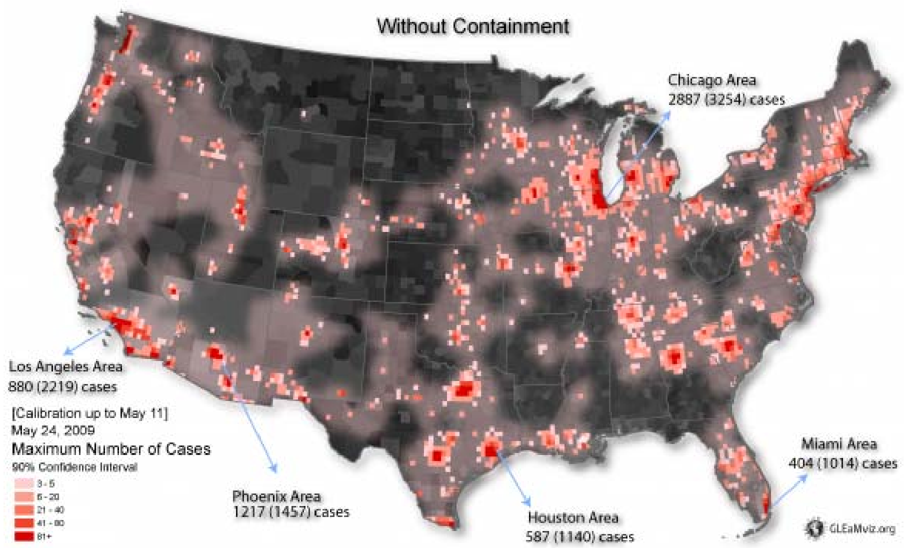
model complexity



predictions



epidemic forecasts ???



- fluid and gas masses
- physical laws

- satellites

- large systems non-linear eqs
- supercomputer infrastructures for weather forecasts

- heterogeneous individuals
- social behavior & infection process

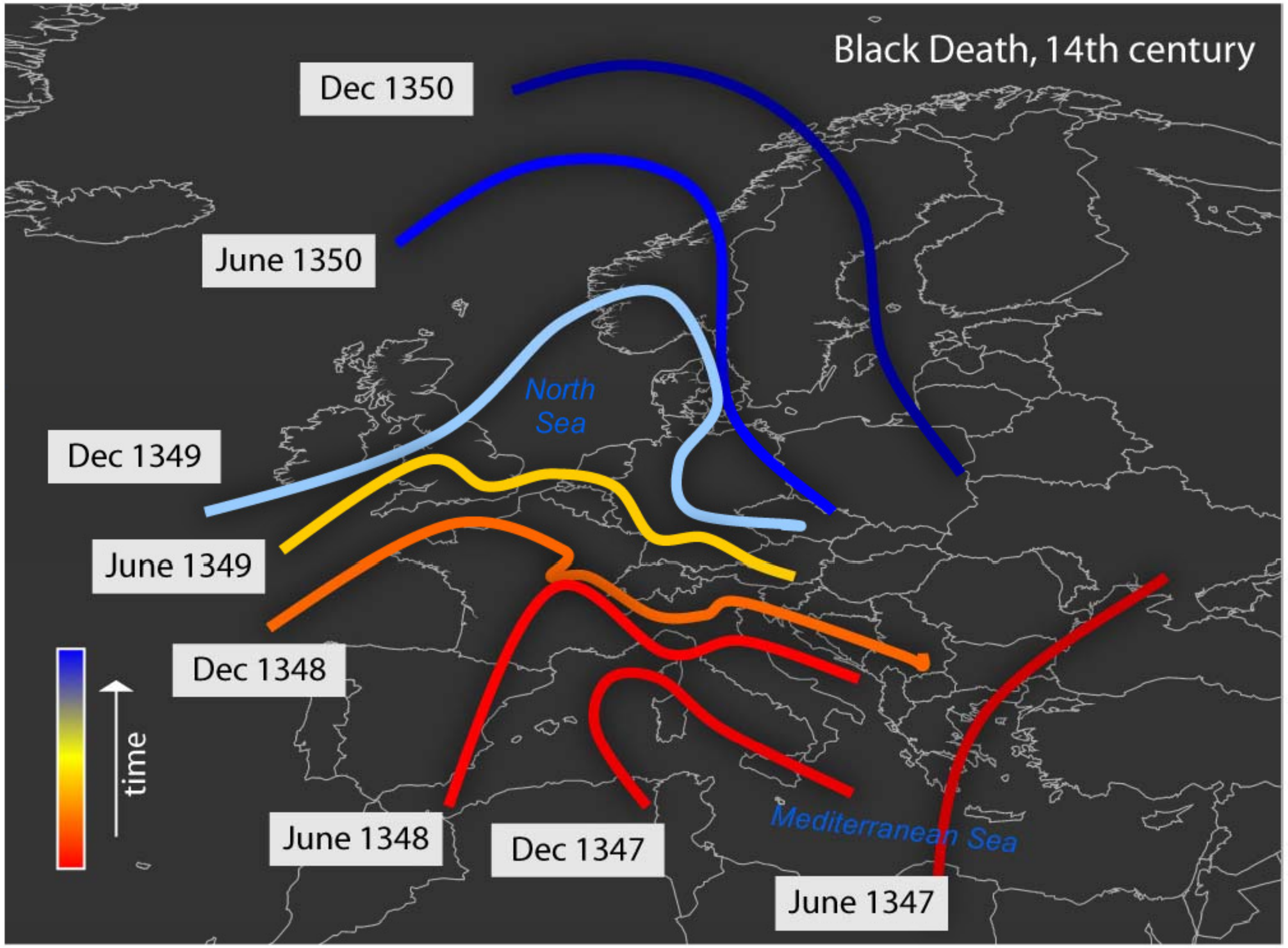
feasible?

- ✓ development of new informatics tools
- ✓ tremendous progress in data gathering
  - ✘ cell phones, GPSs, embedded sensor technologies, …
- ✓ increase in computational power

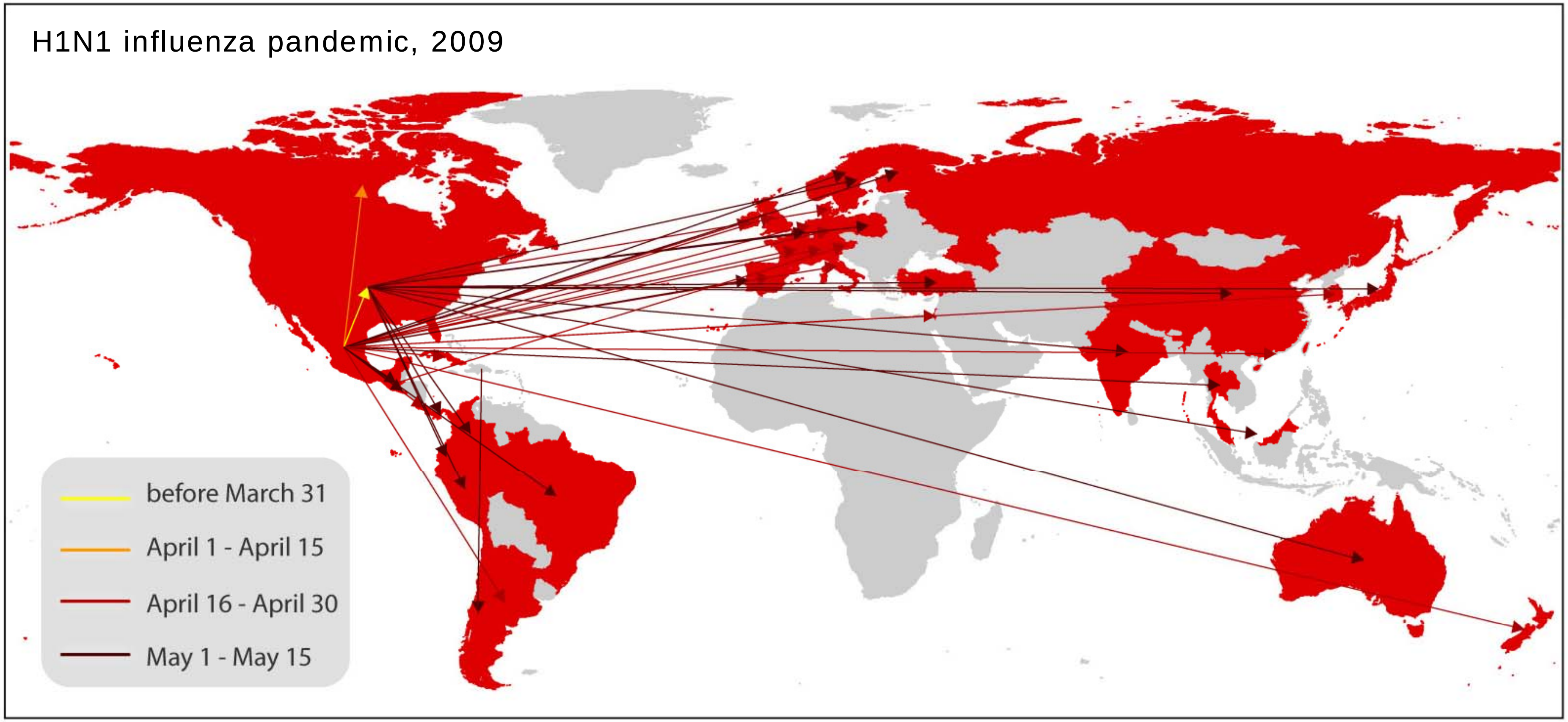
collection, analysis, integration and visualization of huge flows of quantitative demographic, social, geographic, behavioral datasets

✘ ***large-scale models***

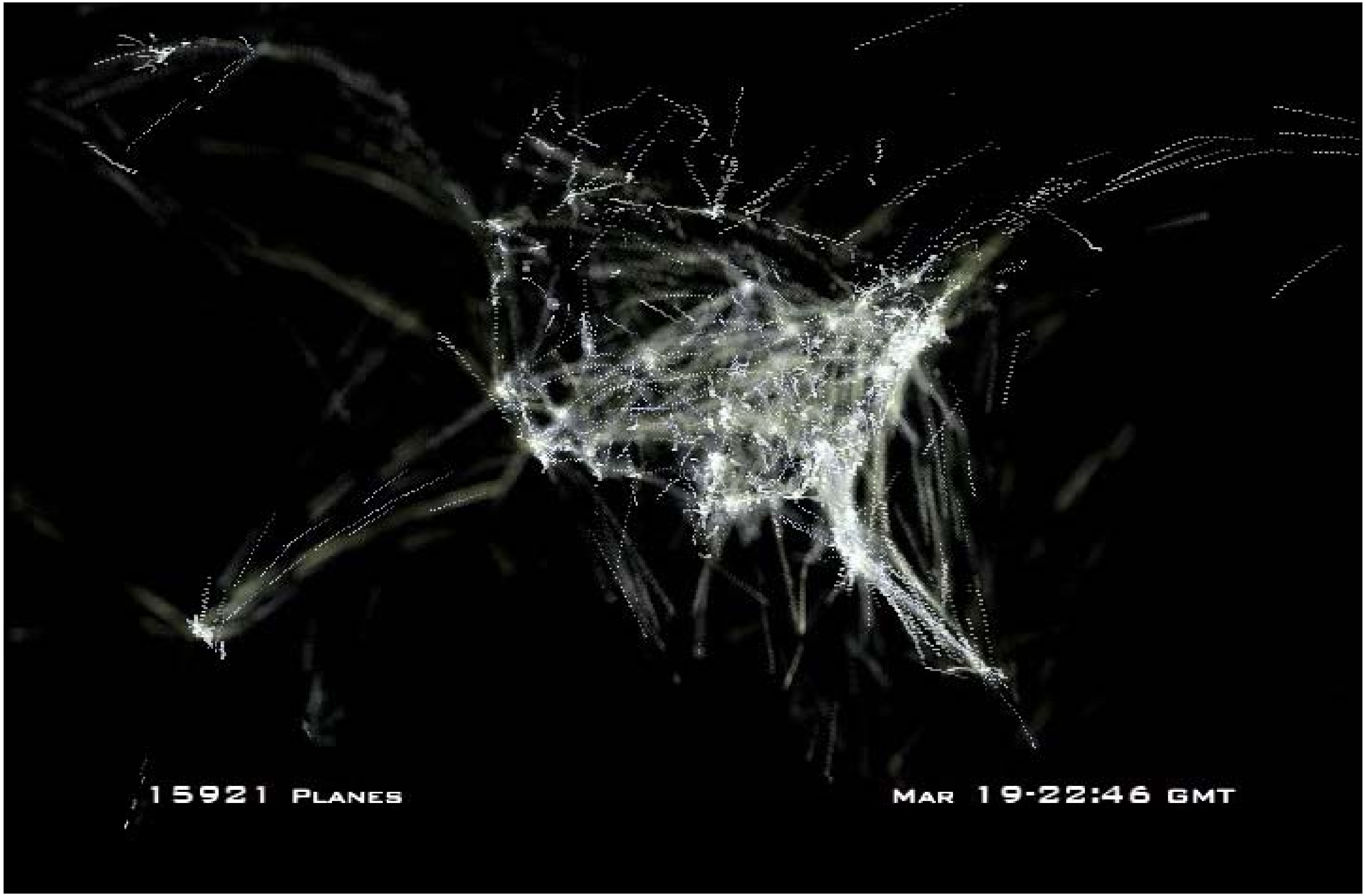
ingredients: people, mobility



ingredients: people, mobility

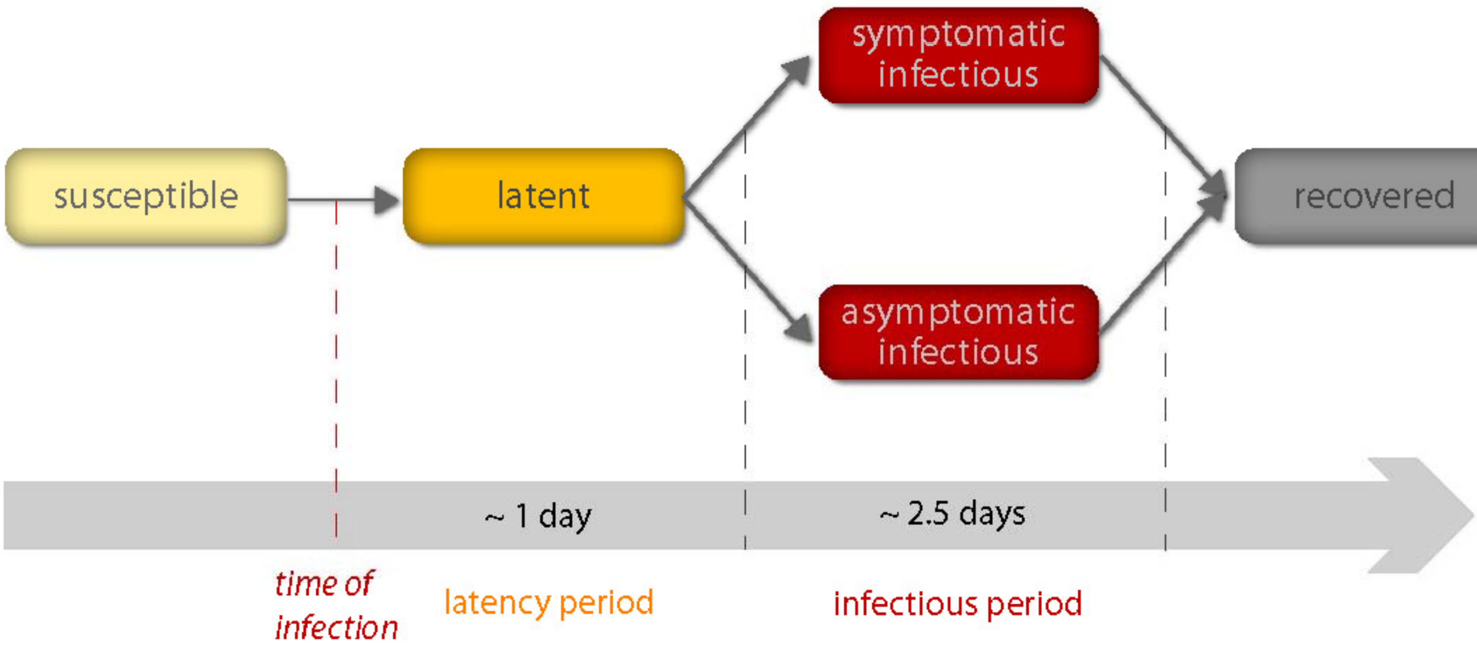


air travel



ingredients: people, disease model

influenza-like-illness



GLEaM – GLobal Epidemic and Mobility model

Geographical resolution

Population layer

Population Distribution

- resolution 15’x15’ arc
- data source: SEDAC (Columbia University)

Mobility layers

Commuting Network

census data for >30 countries in 5 continents, extended to all the countries

World Airport Network

- 3362 airports in 220 countries
- 16842 connections with travel flows
- more than 99 % of the global commercial traffic
- data source: IATA, OAG

Balcan, Colizza et al. PNAS (2009).

GLEaMviz.org

GLEaM overview

equations...

infection

air-travel

$$X_j^{[m]}(t+\Delta t) - X_j^{[m]}(t) = \Delta X_j^{[m]} + \Omega_j([m])$$

number of individuals
in compartment [m]
in subpopulation j

Balcan et al. JoCS (2010).

integration of air travel operator

$$X_j^{[m]}(t+\Delta t) - X_j^{[m]}(t) = \Delta X_j^{[m]} + \boxed{\Omega_j([m])}$$

$$\tilde{\omega}_{j\ell} = \omega_{j\ell}[\alpha + \eta(1-\alpha)]$$ chance in flight occupancy from j to l

$$p_{j\ell} = \tilde{\omega}_{j\ell}\Delta t / N_j$$ probability of flying from j to l

multinomial distribution for passengers flying from j to l

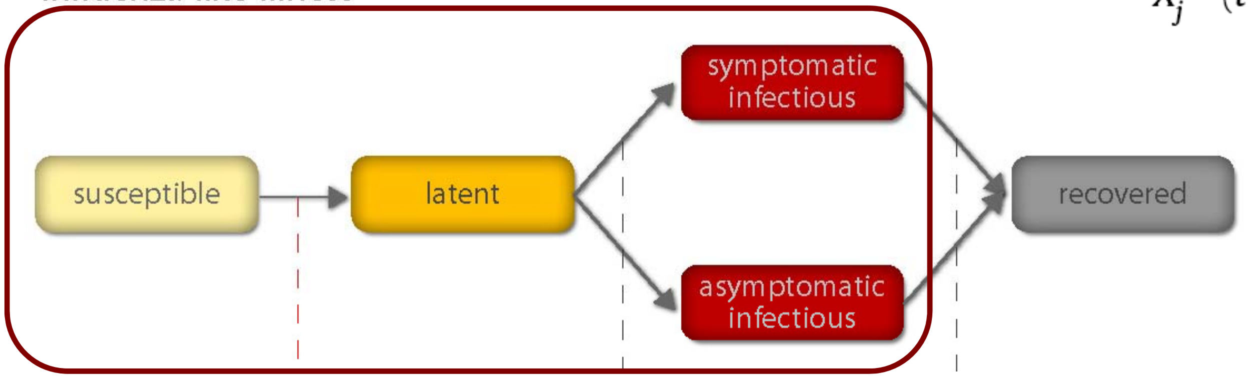
$$P(\{\xi_{j\ell}\}) = \frac{X_j^{[m]}!}{(X_j^{[m]} - \sum_\ell \xi_{j\ell})! \prod_\ell \xi_{j\ell}!} \prod_\ell p_{j\ell}^{\xi_{j\ell}} \times \left(1 - \sum_\ell p_{j\ell}\right)^{(X_j^{[m]} - \sum_\ell \xi_{j\ell})}$$

$$\Omega_j([m]) = \sum_\ell (\xi_{\ell j}(X_\ell^{[m]}) - \xi_{j\ell}(X_j^{[m]}))$$

integration of epidemic operator

$$X_j^{[m]}(t+\Delta t) - X_j^{[m]}(t) = \Delta X_j^{[m]} + \Omega_j([m])$$

influenza-like-illness



$$\Delta X_j^{[m]} = \sum_{[n]} \{-\mathcal{D}_j([m],[n]) + \mathcal{D}_j([n],[m])\}$$

from [m] to [n]; from [n] to [m]

for latent individuals:

$$\Delta L_j(t) = -\left[\mathcal{D}_j(L, I^a) + \mathcal{D}_j(L, I^t) + \mathcal{D}_j(L, I^{nt})\right] + \mathcal{D}_j(S, L).$$

$$Pr^{Bin}(S_j(t), p_{S_j \to L_j})$$

$$p_{S_j \to L_j} = \lambda_j \Delta t$$

generation of new infections

λ_j = force of infection

force of infection

- within the city
- with neighbor cities through commuting

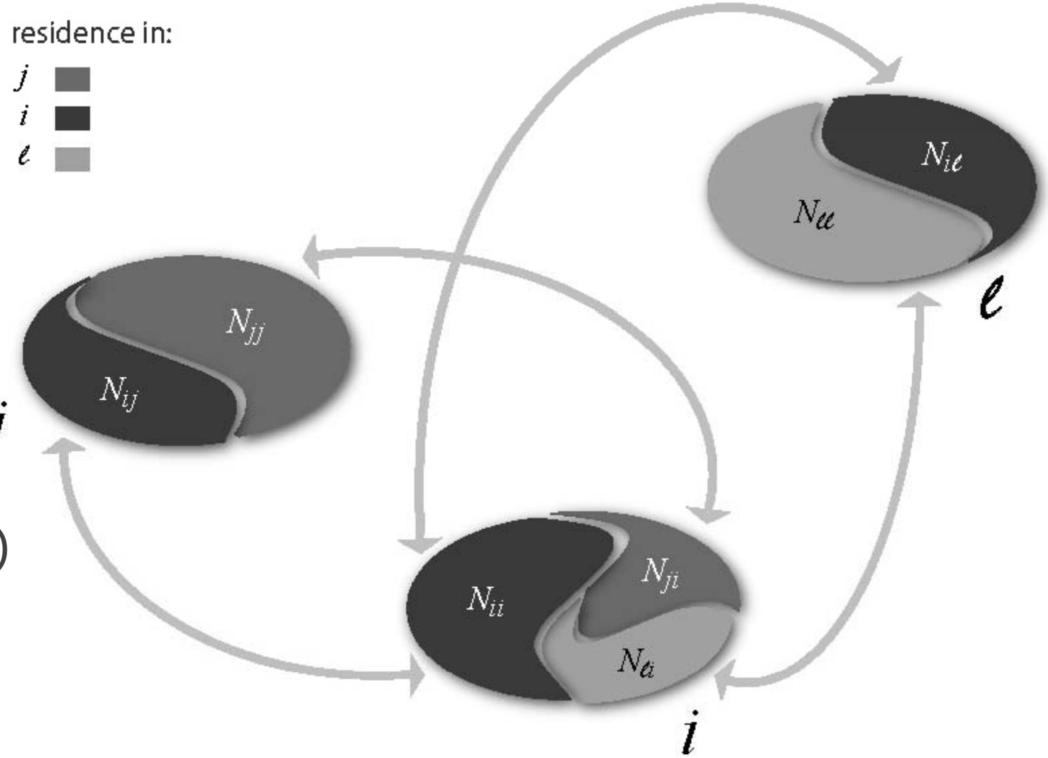
↓

time-scale separation technique (commuting is fast!)

$$\lambda_j = \frac{\lambda_{jj}}{1+\sigma_j/\tau} + \sum_i \frac{\lambda_{ji}\sigma_{ji}/\tau}{1+\sigma_j/\tau}.$$

$$\lambda_{jj} = \frac{\beta_j}{N_j^*}\left(I_{jj}^{nt} + I_{jj}^{t} + r_\beta I_{jj}^{a}\right) + \frac{\beta_j}{N_j^*}\sum_i \left(I_{ij}^{nt} + I_{ij}^{t} + r_\beta I_{ij}^{a}\right)$$

$$\lambda_{ji} = \frac{\beta_i}{N_i^*}\left(I_{ii}^{nt} + I_{ii}^{t} + r_\beta I_{ii}^{a}\right) + \frac{\beta_i}{N_i^*}\sum_{\ell \in \upsilon(i)} \left(I_{\ell i}^{nt} + I_{\ell i}^{t} + r_\beta I_{\ell i}^{a}\right)$$



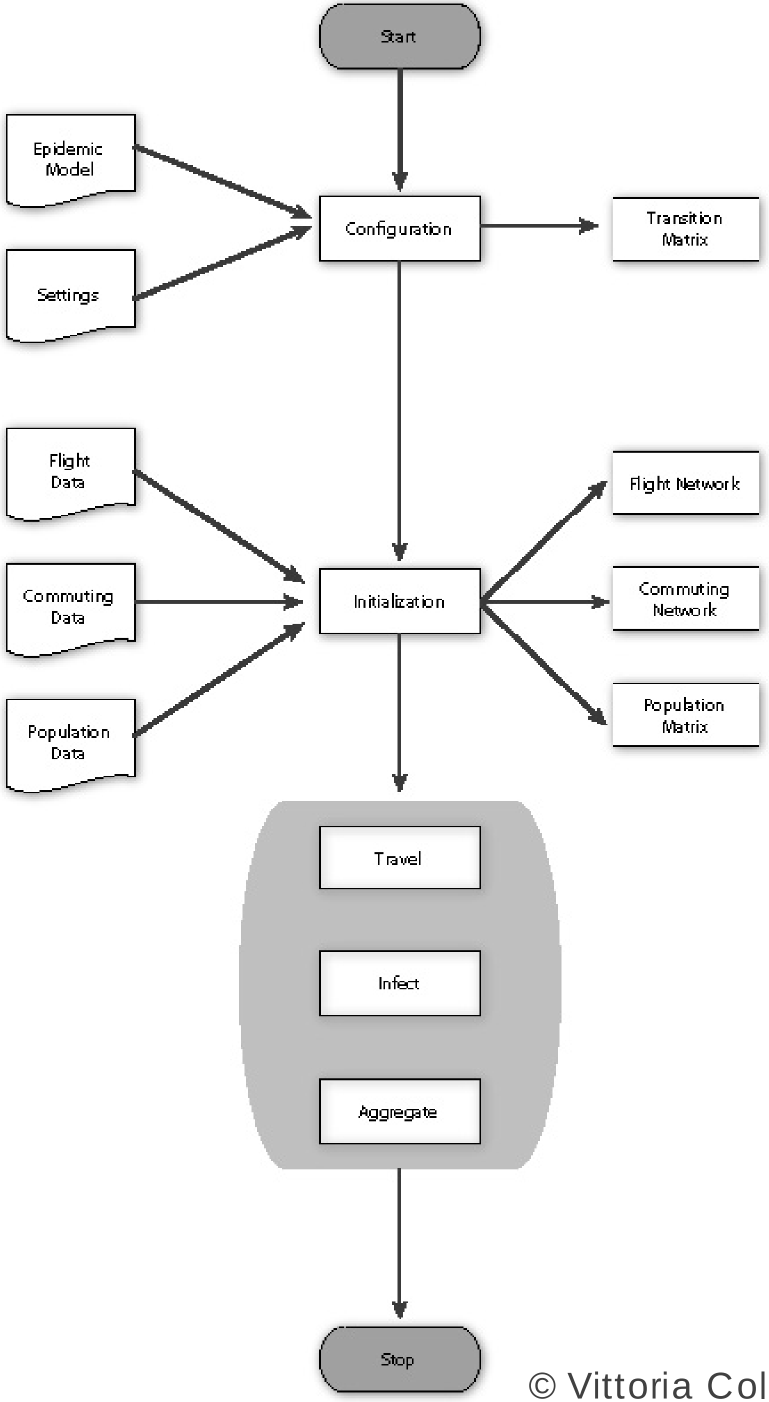
algorithm

Algorithm 1.

Parse model file
Load data input files:
  population database
  commuting
  flight networks

foreach timestep *t*:
do
  Flight connections (See Algorithm 2)
  Infect (See Algorithm 3)
  Aggregate results for each detail level.
done

Generate final output



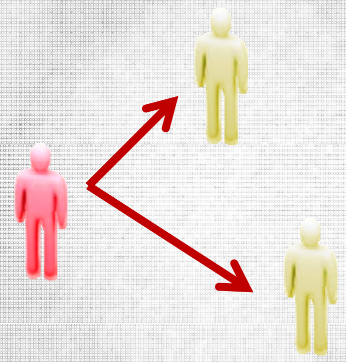
Balcan et al. JoCS (2010).

GLEaM @ work: H1N1 pandemic

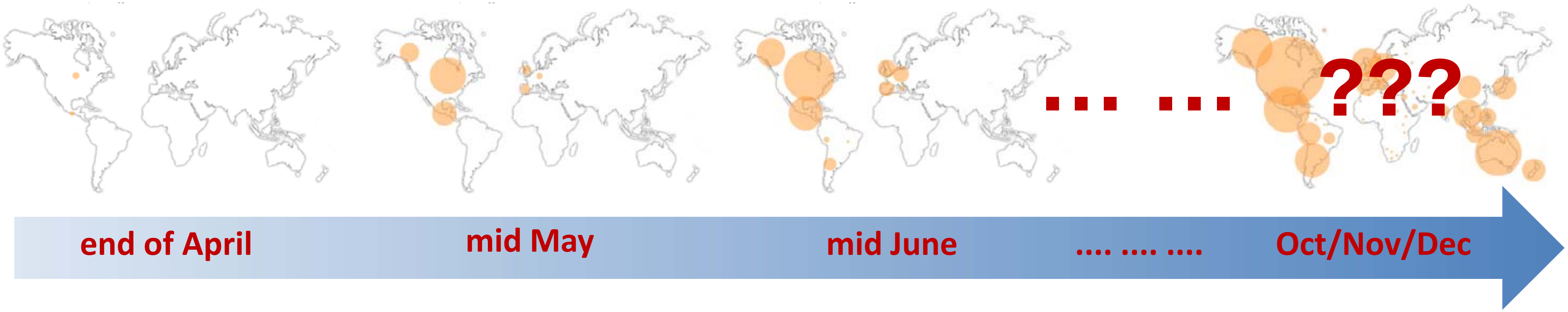
predictions ???

the unknown

- genome
- incubation period, infectious period
- transmission potential, R_0
- pathogenicity
- attack rate by age classes
- mortality
- seasonality
- spreading pattern
- mutation
- … …



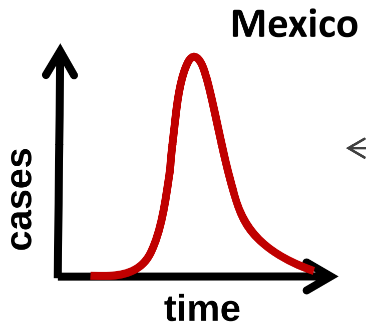
the problem

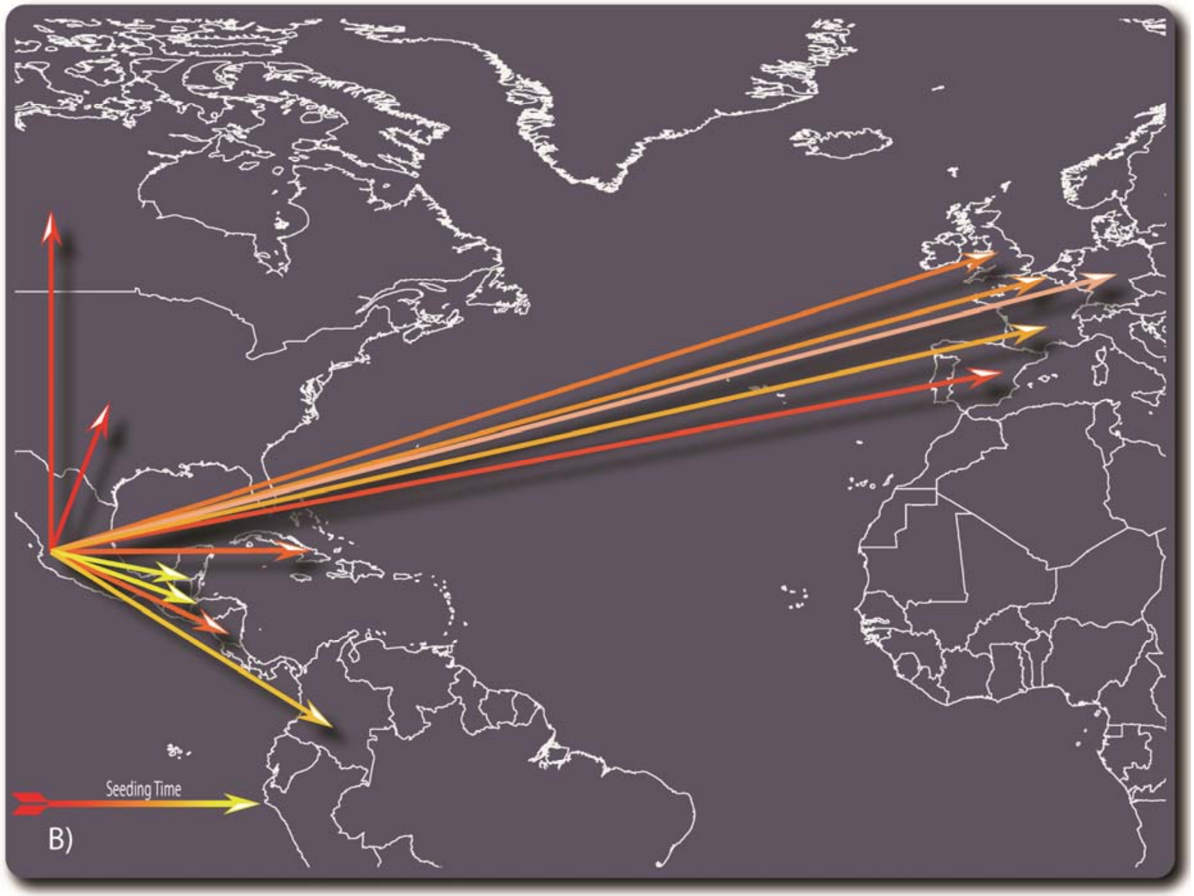


our solution: ***global epidemic & mobility model***

- ❑ transmission potential, R_0
- ❑ seasonality

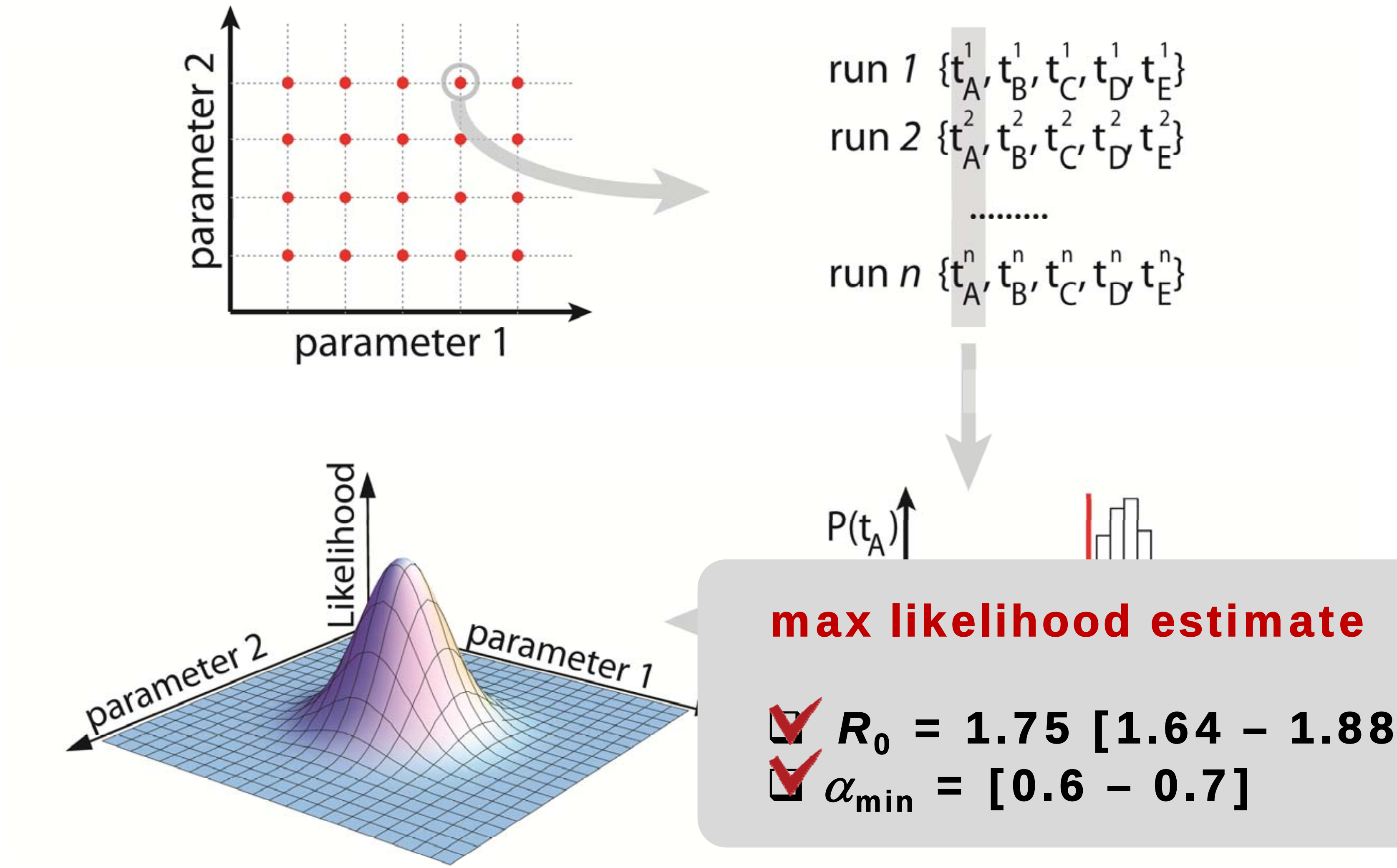
R_0 estimation on empirical arrival times





Balcan et al, BMC Medicine (2009)

Monte carlo likelihood analysis



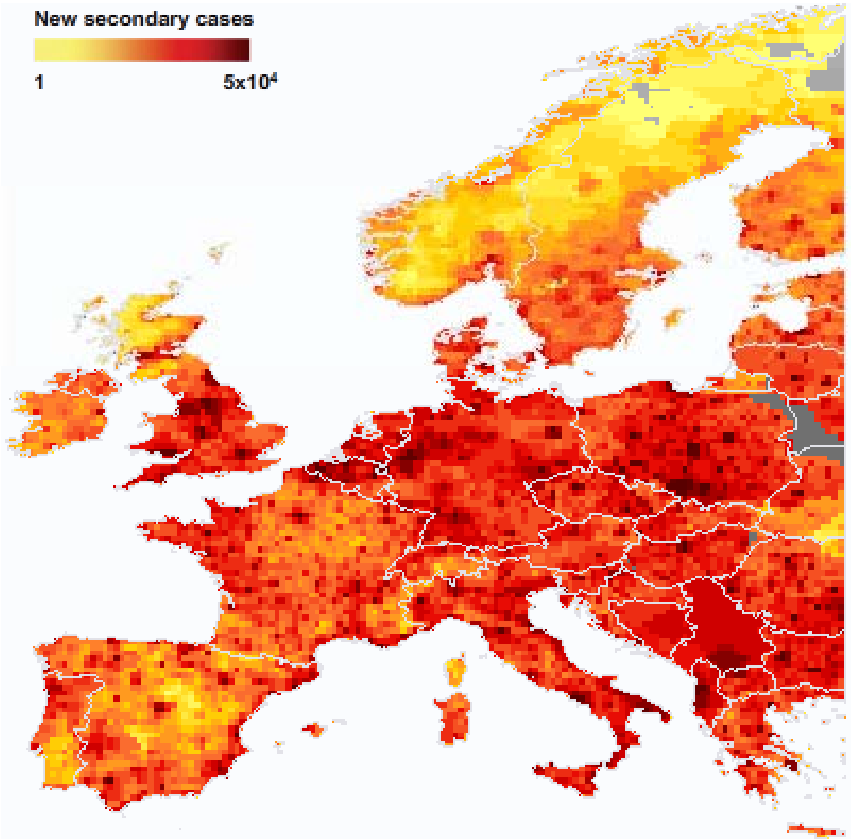
max likelihood estimate

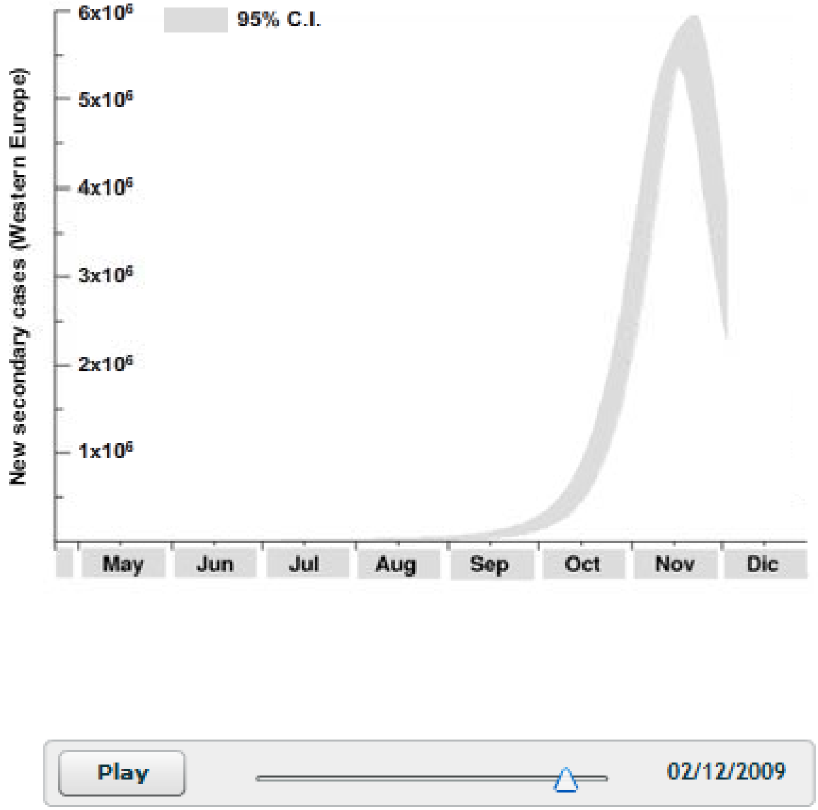
- ☑ R_0 = 1.75 [1.64 – 1.88]
- ☑ α_{min} = [0.6 – 0.7]

Balcan et al, BMC Medicine (2009)

predictions for Europe

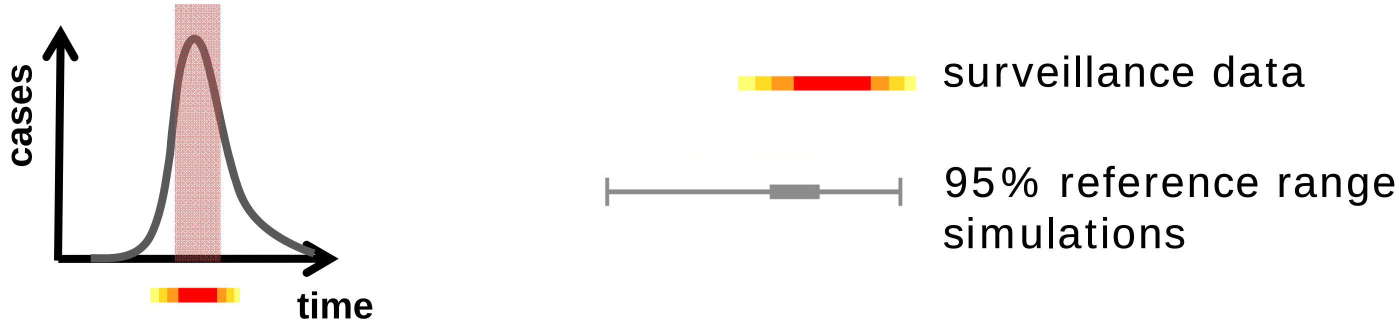
No intervention scenario

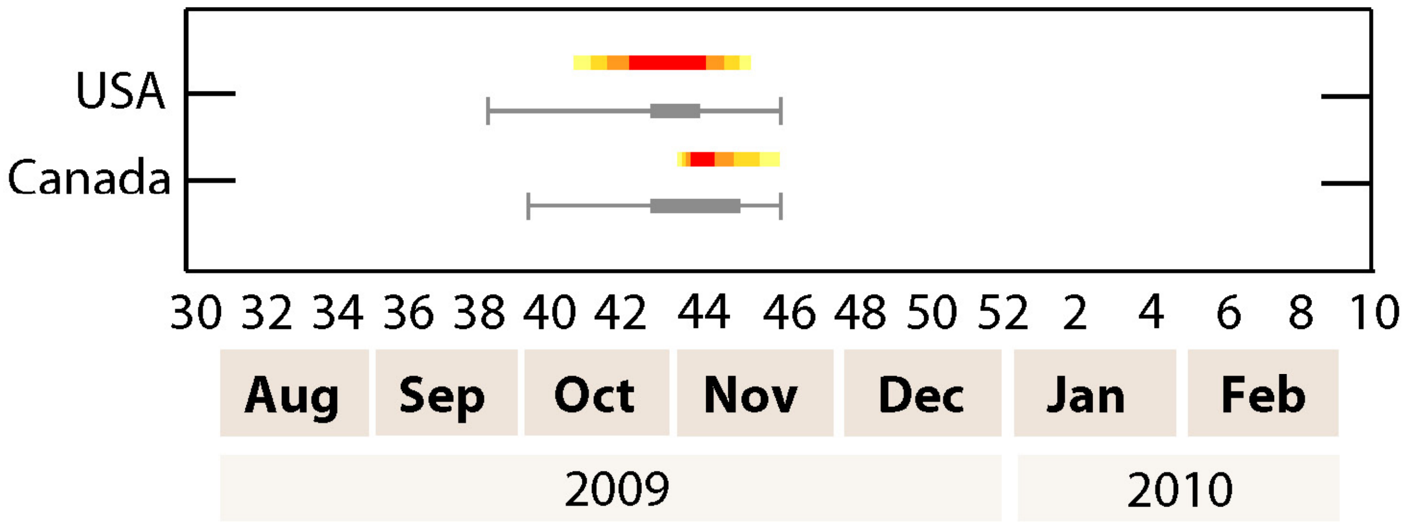




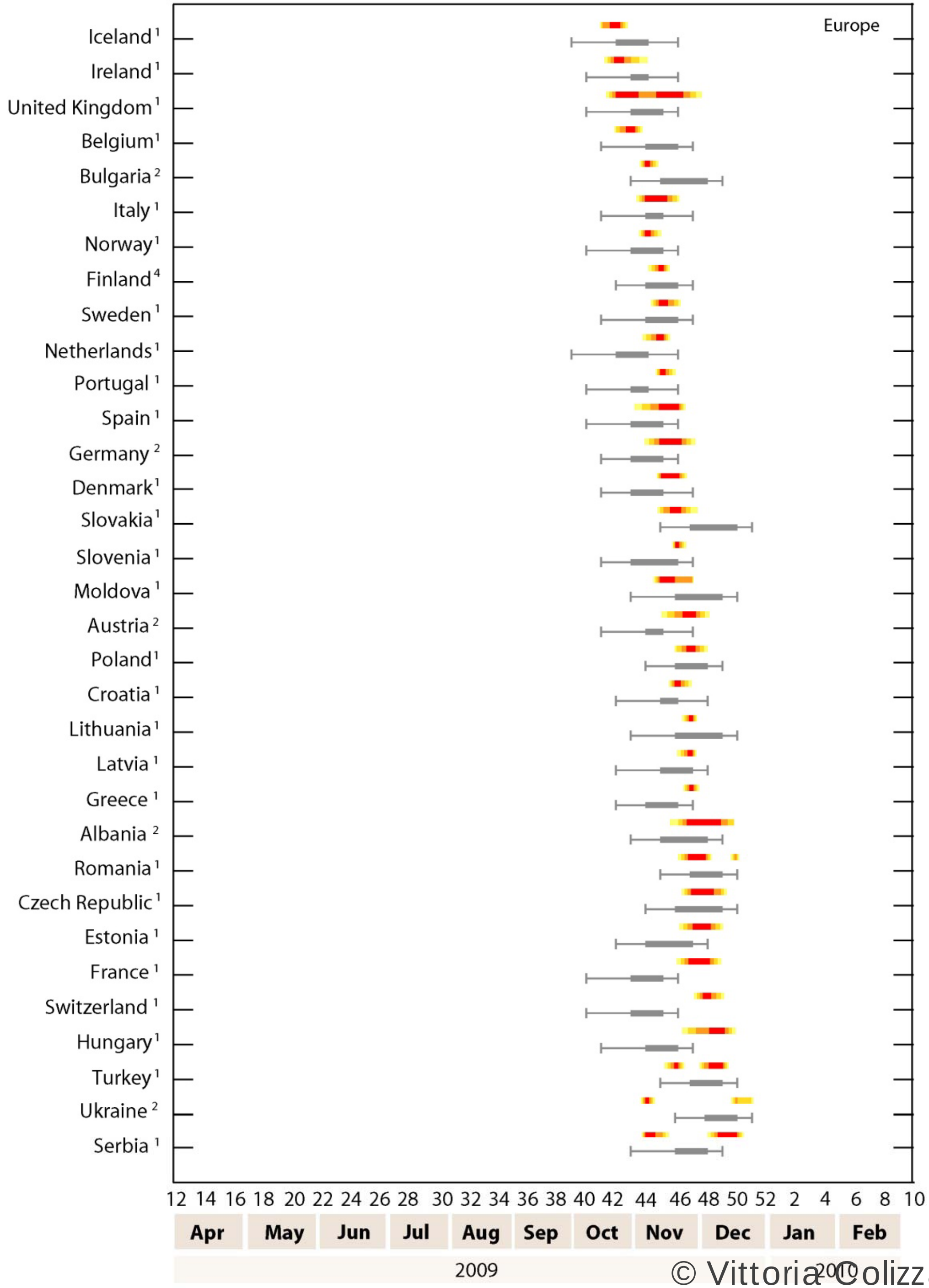
Balcan et al. BMC Medicine (2009)

comparison with data





comparison with data



CPU requirements and data production

INDIANA UNIVERSITY

UNIVERSITY INFORMATION TECHNOLOGY SERVICES / RESEARCH TECHNOLOGIES

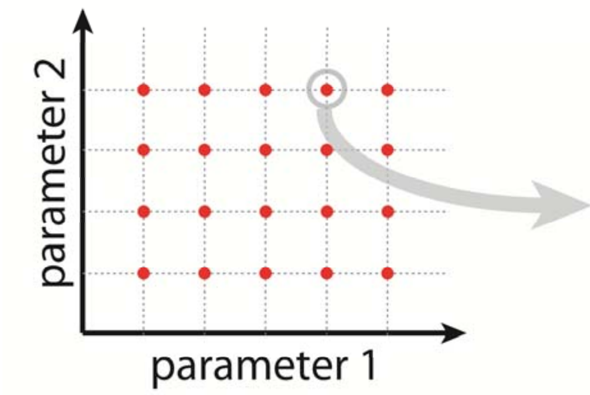
High Performance Systems

Systems
- Big Red
- Quarry
- Research Database Complex

Search

The Big Red Cluster

- 2006: most powerful computer in US university
- 2006: among 50 fastest in the world
- theoretical peak performance: >40 teraflops
- achieved >28 teraflops on numerical computations



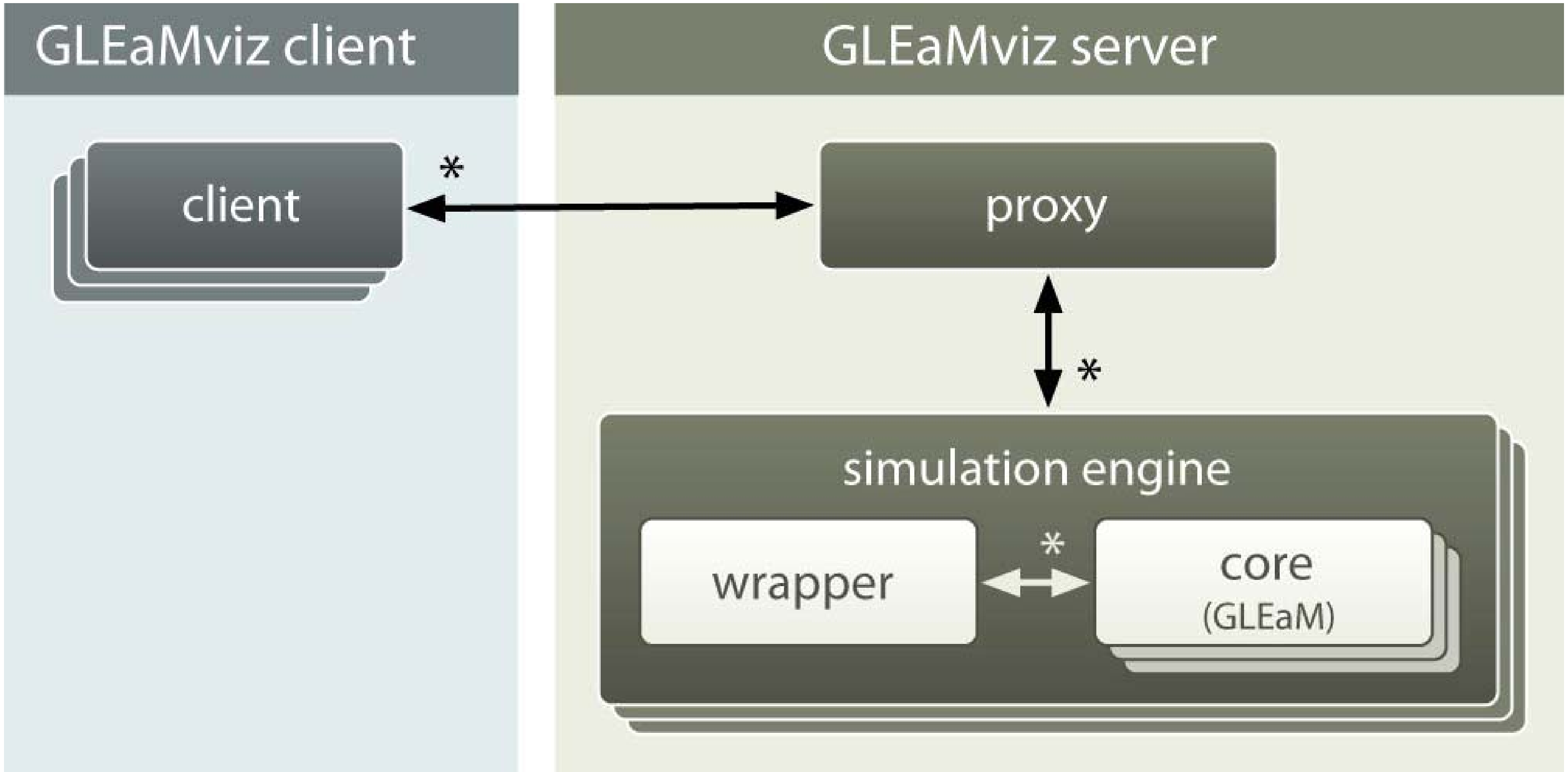
- 256 nodes, 4 cores
- May – August
- ~ 50 TB data

H1N1 = warming up exercise...

...tool for public health crisis?

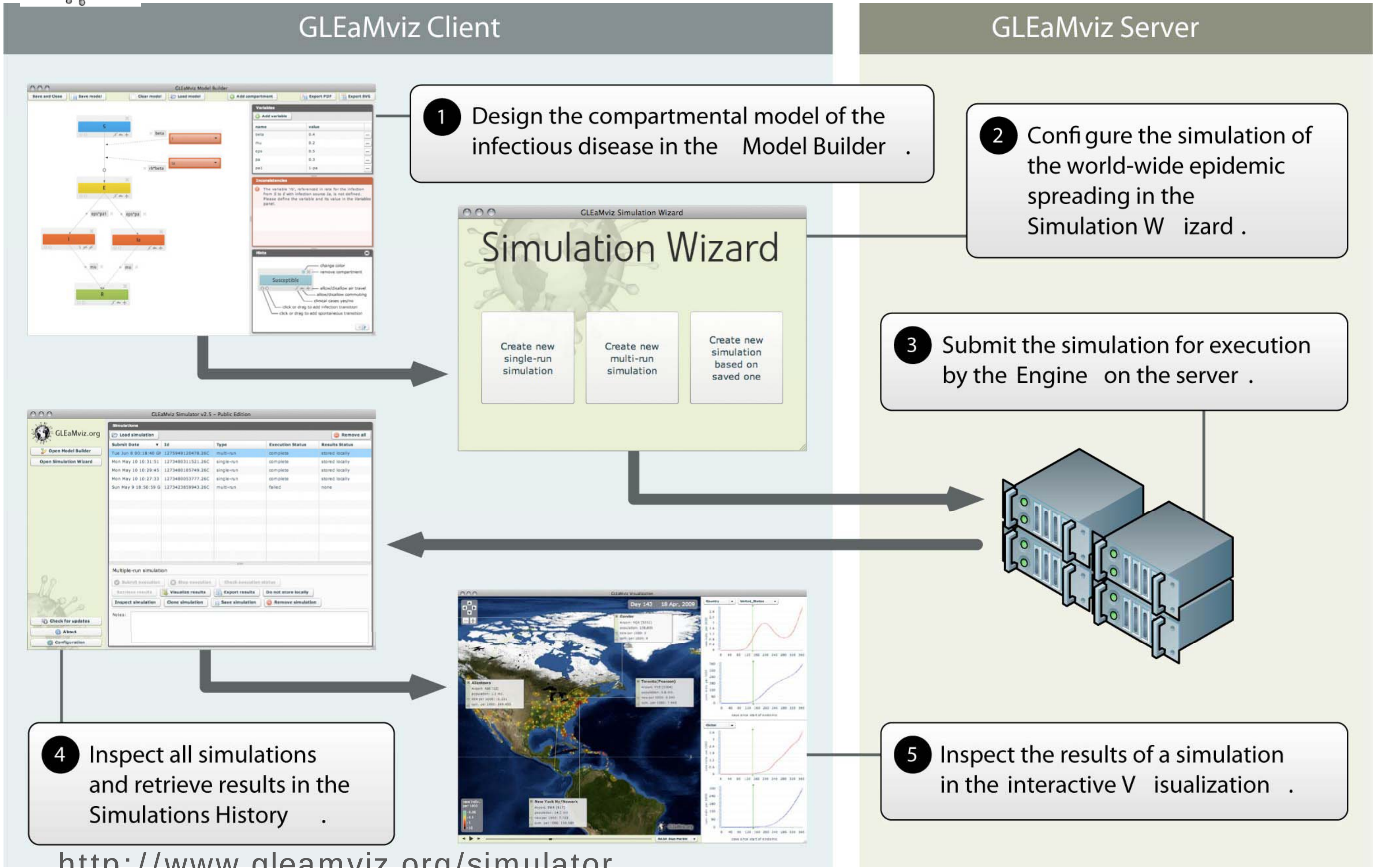
complex sophisticate realistic models	⇔	flexible computationally feasible accessible easy to use

GLEaMviz Simulator: architecture



http://www.gleamviz.org/simulator

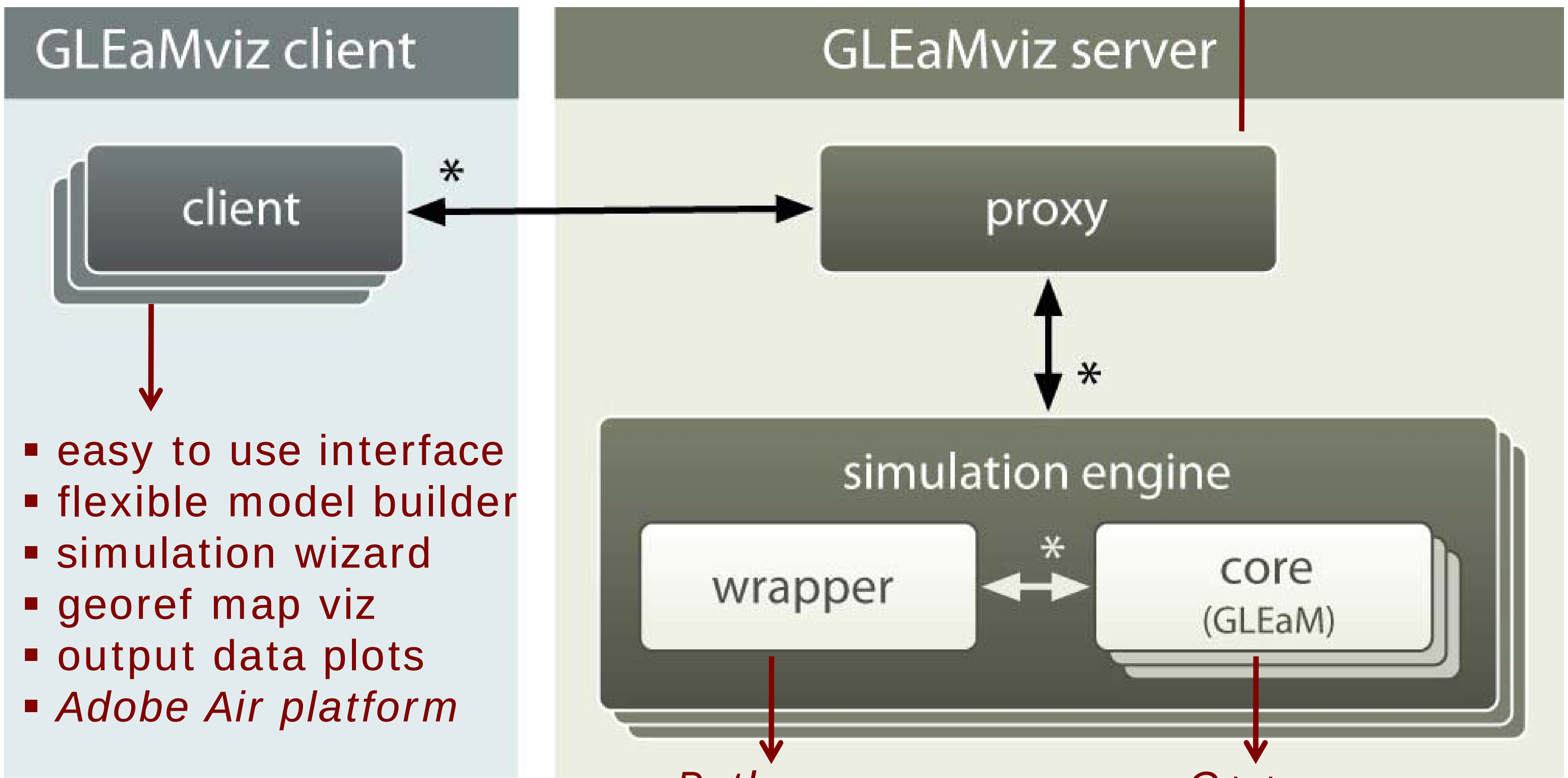
GLEaMviz Simulator: workflow



http://www.gleamviz.org/simulator

elements

- manage client connections
- custom protocol for commands and data
- run engine instances
- configurable setup
- *Python*



- easy to use interface
- flexible model builder
- simulation wizard
- georef map viz
- output data plots
- *Adobe Air platform*

- *Python*
- core execution
- multi-run analysis

- *C++*
- stochastic computation

application example:

pandemic emerging in Naples...

epidemics in 21st century

Science AAAS

EDITORIAL

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

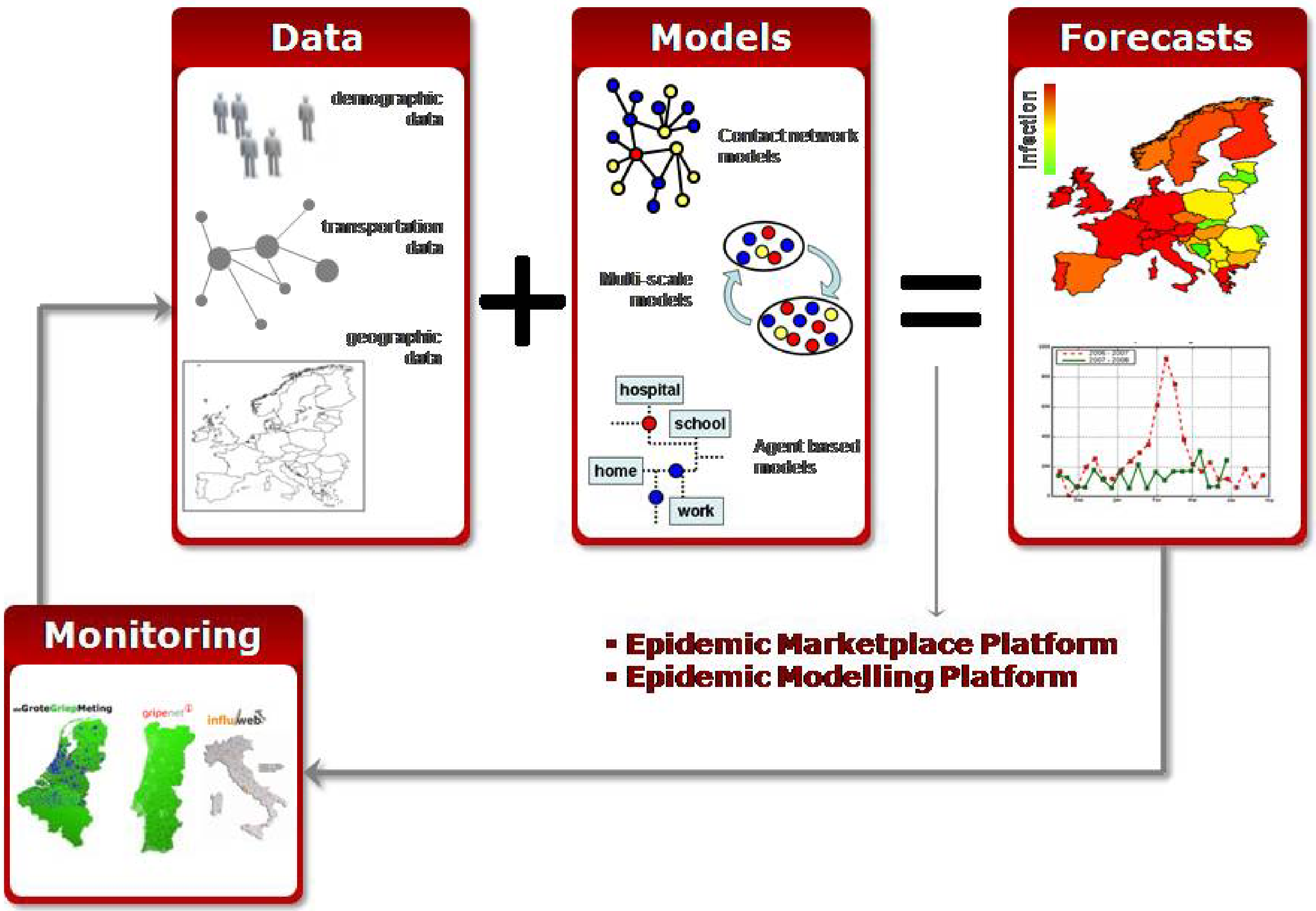
FEW SITUATIONS MORE DRAMATICALLY ILLUSTRATE THE SALIENCE OF SCIENCE TO POLICY THAN AN epidemic. The relevant science takes place rapidly and continually, in the laboratory, clinic, and community. In facing the current swine flu (H1N1 influenza) outbreak, the world has benefited from research investment 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 assess-

challenges: **epi**demic frame**work**

EPIWORK



who we are...

acknowledgments

Paolo Bajardi
Daniela Paolotti
Chiara Poletto
Jose J. Ramasco
Michele Tizzoni
Wouter Van den Broeck

INSTITUTE FOR SCIENTIFIC INTERCHANGE FOUNDATION

Duygu Balcan
Bruno Goncalves
Hao Hu
Nicola Perra
Alessandro Vespignani

INDIANA UNIVERSITY

GLEaMviz.org

http://vcolizza.googlepages.com
http://www.epifor.eu
http://www.gleamviz.org/simulator

EpiFor erc SEVENTH FRAMEWORK PROGRAMME

EPIWORK SEVENTH FRAMEWORK PROGRAMME

DYNANETS SEVENTH FRAMEWORK PROGRAMME