

CONTAGIONS OVER MULTIPLEX NETWORKS: THE ROLE OF AI AND COMPUTING

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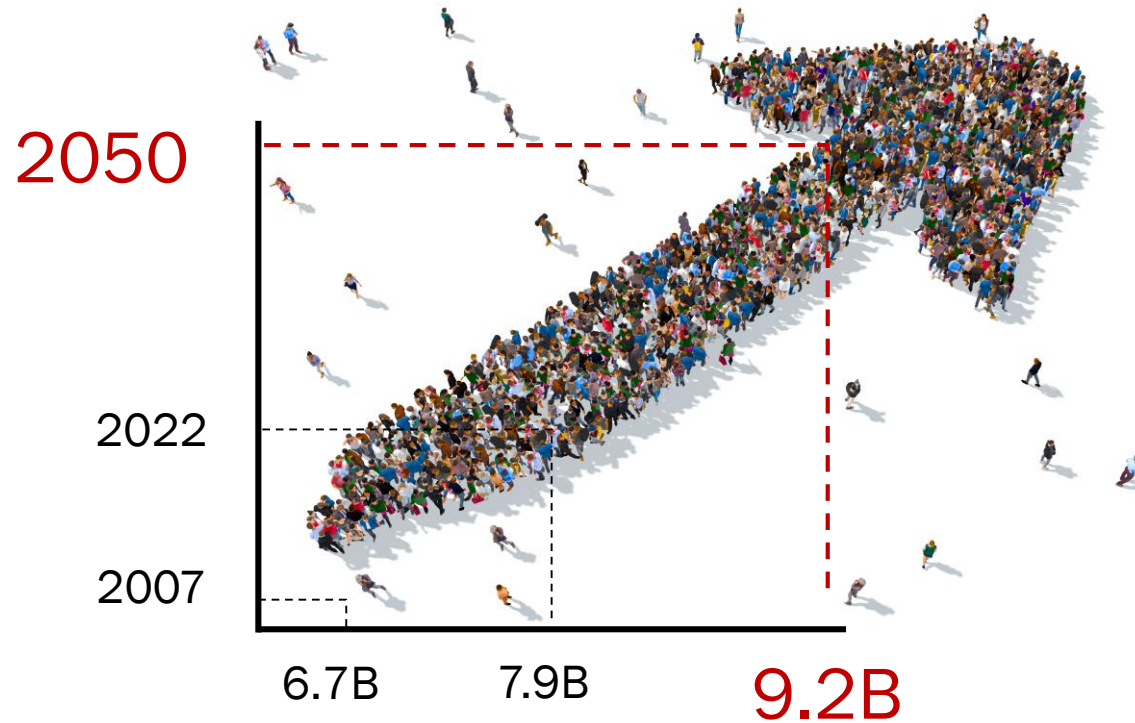
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Population Growth, Megacities & Small-World Effect

By 2050: 27 Megacities in the world with 10M+ people (up from 19 in 2022)

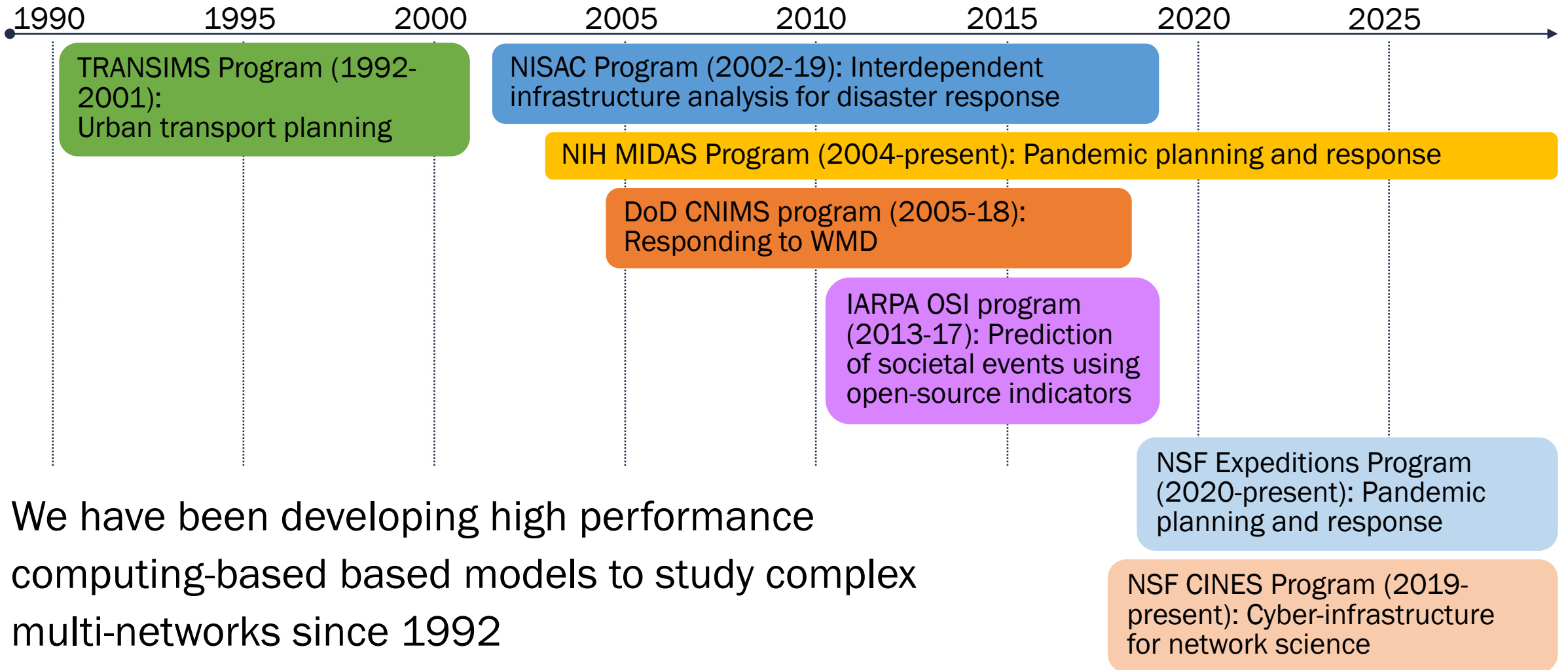


Multiplexed networks and the society they support co-evolve



Creates unprecedented opportunities. They also pose potential risks to the global environment, resilience, social stability, the national development of poorer countries and can result in inequitable allocation of resources putting the marginalized groups at further risk.

A brief history



We have been developing high performance computing-based based models to study complex multi-networks since 1992

How can one detect, assess and reduce the impact of a pandemic outbreak such as COVID-19?

<https://covid19.biocomplexity.virginia.edu/>

References



DOI:10.1145/2483852.2483871

The challenge of developing and using computer models to understand and control the diffusion of disease through populations.

BY MADHAV MARATHE AND ANIL KUMAR S. VULLIKANTI

Computational Epidemiology

AN EPIDEMIC IS said to arise in a community or region when cases of an illness or other health-related events occur in excess of normal expectancy. Epidemics are considered to have influenced significant historical events, including the plagues in Roman times and Middle Ages, the fall of the Han empire in the 3rd century in China, and the defeat of the Aztecs in the 1500s, due to a smallpox outbreak.⁹ The 1918 flu pandemic in the U.S. was responsible for more deaths than those due to World War I. The last 50 years have seen epidemics caused by HIV/AIDS, SARS, and influenza-like illnesses. Despite significant medical advances, according to the World Health Organization (WHO), infectious diseases account for more than 13 million deaths a year.⁴⁴

Societal interest in controlling outbreaks is probably just as old as the diseases themselves. Interestingly, it appears the Indians and Chinese knew the idea of variolation to control smallpox as early as the 8th century A.D. Epidemiology is a formal branch of science focusing on the study of space-time patterns of illness in a population and the factors that lead to these patterns. It plays an essential role in public health by

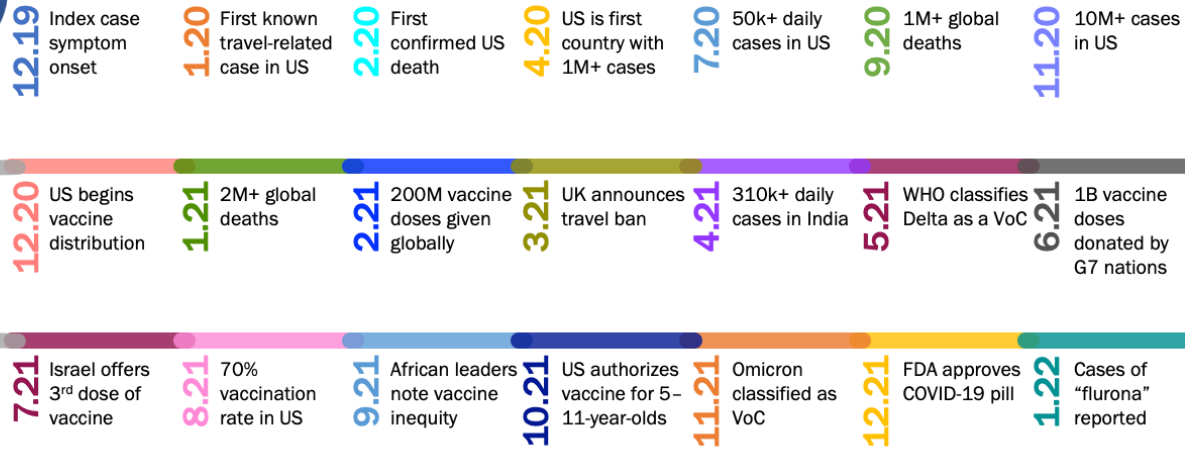
» key insights

- Controlling and responding to future pandemics will be challenging due to a number of emerging global trends including increased and denser urbanization, increased local as well as global travel, and a generally older and immuno-compromised population.
- Public health epidemiology is a complex system problem. Epidemics, social-contact networks, individual and collective behavior, and public policies coevolve during a pandemic—a system-level understanding must represent these components and their coevolution.
- Mathematical and computational models of social networks and epidemic spread and methods to analyze them are critical in public health epidemiology.
- Advances in computing, big data, and computational thinking have created entirely new opportunities to support real-time epidemiology.

88 COMMUNICATIONS OF THE ACM | JULY 2013 | VOL. 56 | NO. 7

- *Papers:*

- *CACM 2014:* Computational Epidemiology
- *Nature 2004:* Modelling disease outbreaks in realistic urban social networks.
- *PNAS 2008:* Modeling targeted layered containment of an influenza pandemic in the United States.
- *PNAS 2014:* Opinion: Mathematical models: A key tool for outbreak response.
- Tutorials (KDD'14, AAAI'16, ICSB'17): <https://covid19.biocomplexity.virginia.edu/publications>
- COVID-19 resource page: <https://covid19.biocomplexity.virginia.edu/>
- New NSF Expeditions Project: <https://computational-epidemiology.org>



COVID-19 : How it happened and how did society respond



Why did it become a pandemic

- Zoonosis
- Global connectivity where zoonosis happened
- Silent Spreaders
- Initial response was slow & not decisive (always hard)

Socio political & economic response

- Global unprecedented lock down & travel restrictions
- Trillions of dollars worth of economic stimulus
- Political disagreements led to uncoordinated and decisive response

Scientific and medical response

- 530,000 Preprints from 03/20-09/21
- New treatments (anti-body, plasma)
- New treatment protocols
- Excellent vaccines in a year

Technological response

- New apps for contact tracing
- Genome sequencing completed in record time
- Innovative ways to work, educate, deliver, interact
- HPC consortium formed to support modeling

https://en.wikipedia.org/wiki/Timeline_of_the_COVID-19_pandemic;

<https://www.science.org/content/article/no-revolution-covid-19-boosted-open-access-preprints-are-only-fraction-pandemic-papers>

<https://covid19primer.com/dashboard>

<https://www.who.int/publications/m/item/draft-landscape-of-covid-19-candidate-vaccines>

01-23-2020 All regions Download All FAQ

Cases Vaccine Est.Active Confirmed Deaths Est.Recovered

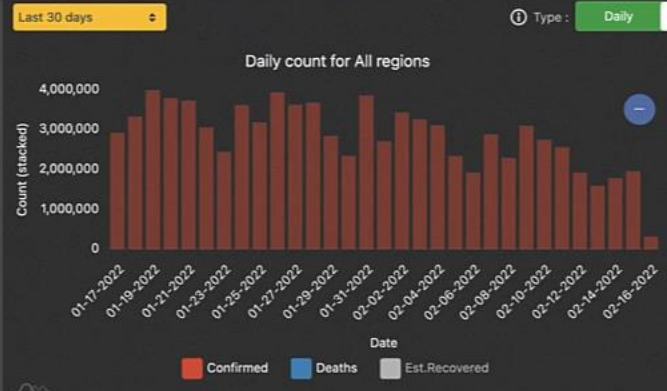
United States: Est.Active: 1 Conf: 1 Deaths: 0 Est.Rec: 0

Time Slider from Jan 22 2020 to Feb 16 2022 Selected Date Jan 23 2020

All regions			
556	556	0	0
Est.Active	Confirmed	Deaths	Est.Recovered

Tutorials: Check USA data by county | Query and filter | more

Analytics Chart Data



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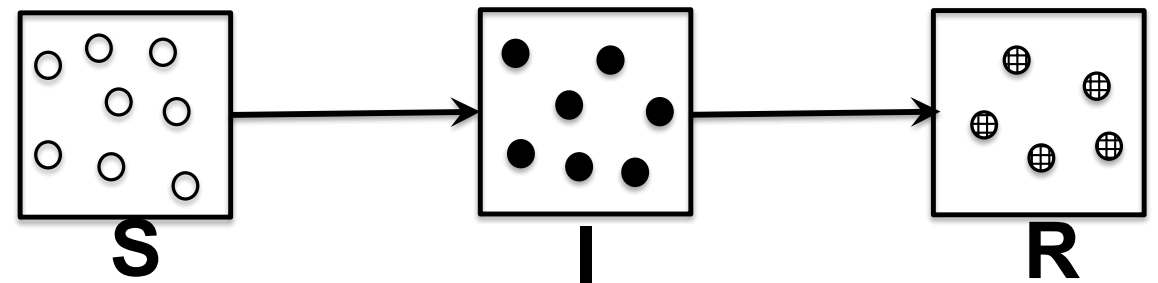
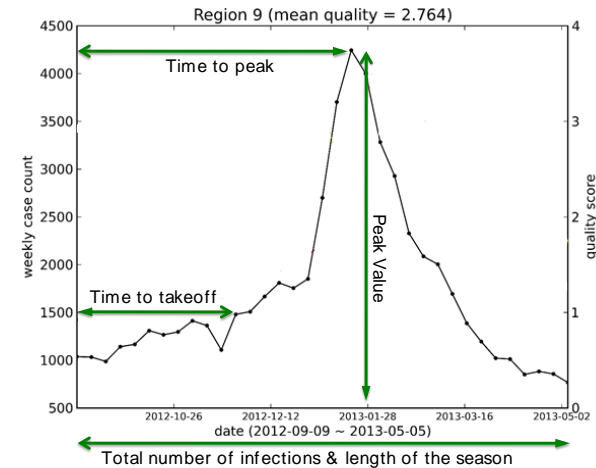
Cumulative number from 4 countries / territories. Last Update : 2020-01-23 03:00:00 (UTC).

Mathematical Models to study Epidemics

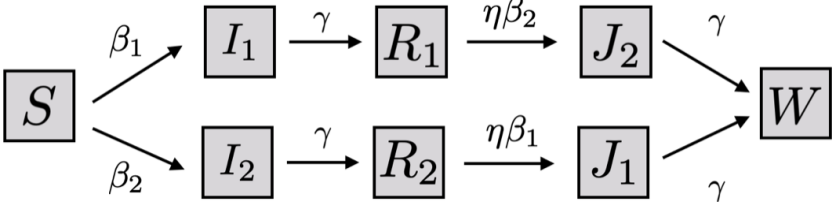
Compartmental mass action models

- Susceptible (S): An individual has never had the disease and is susceptible to being infected
- Infected (I): An individual who currently has the disease and can infect other individuals
- Recovered (R): An individual does not have the disease, cannot infect others, and cannot be infected

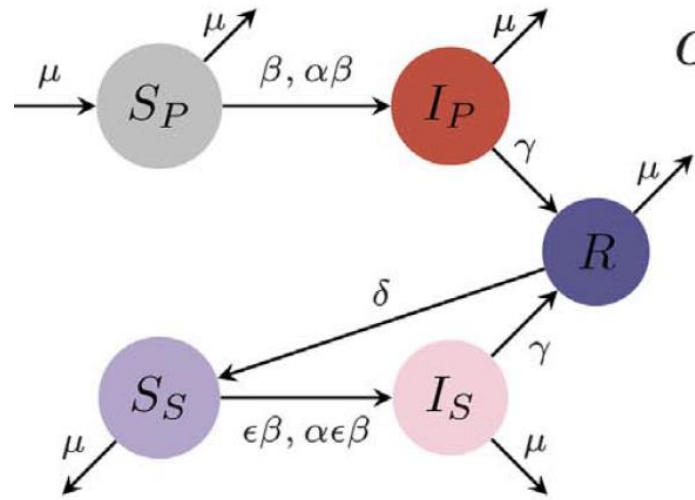
$$\begin{aligned}\frac{ds}{dt} &= -\beta is \\ \frac{di}{dt} &= \beta is - \gamma i \\ \frac{dr}{dt} &= \gamma i\end{aligned}$$



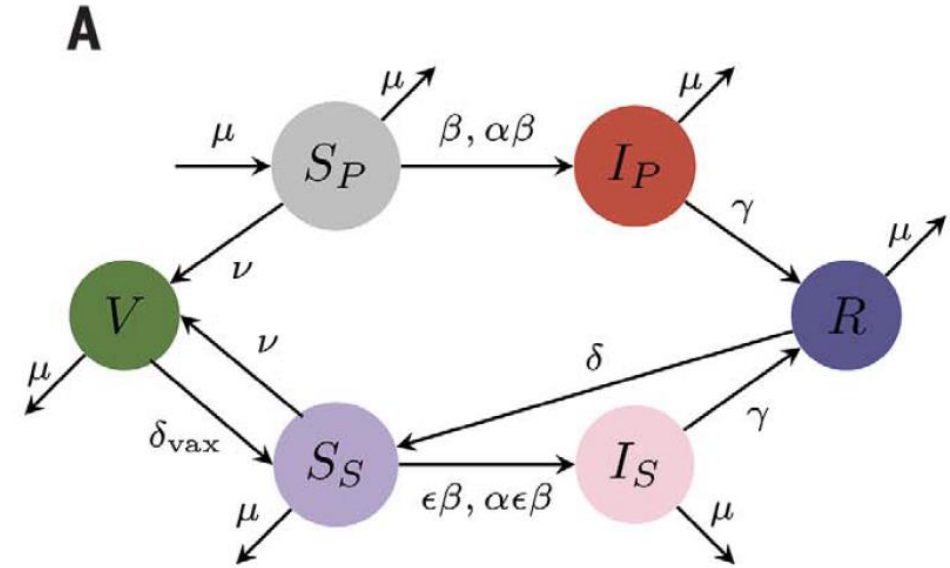
Compartmental mass action models: Extensions



A two strain model



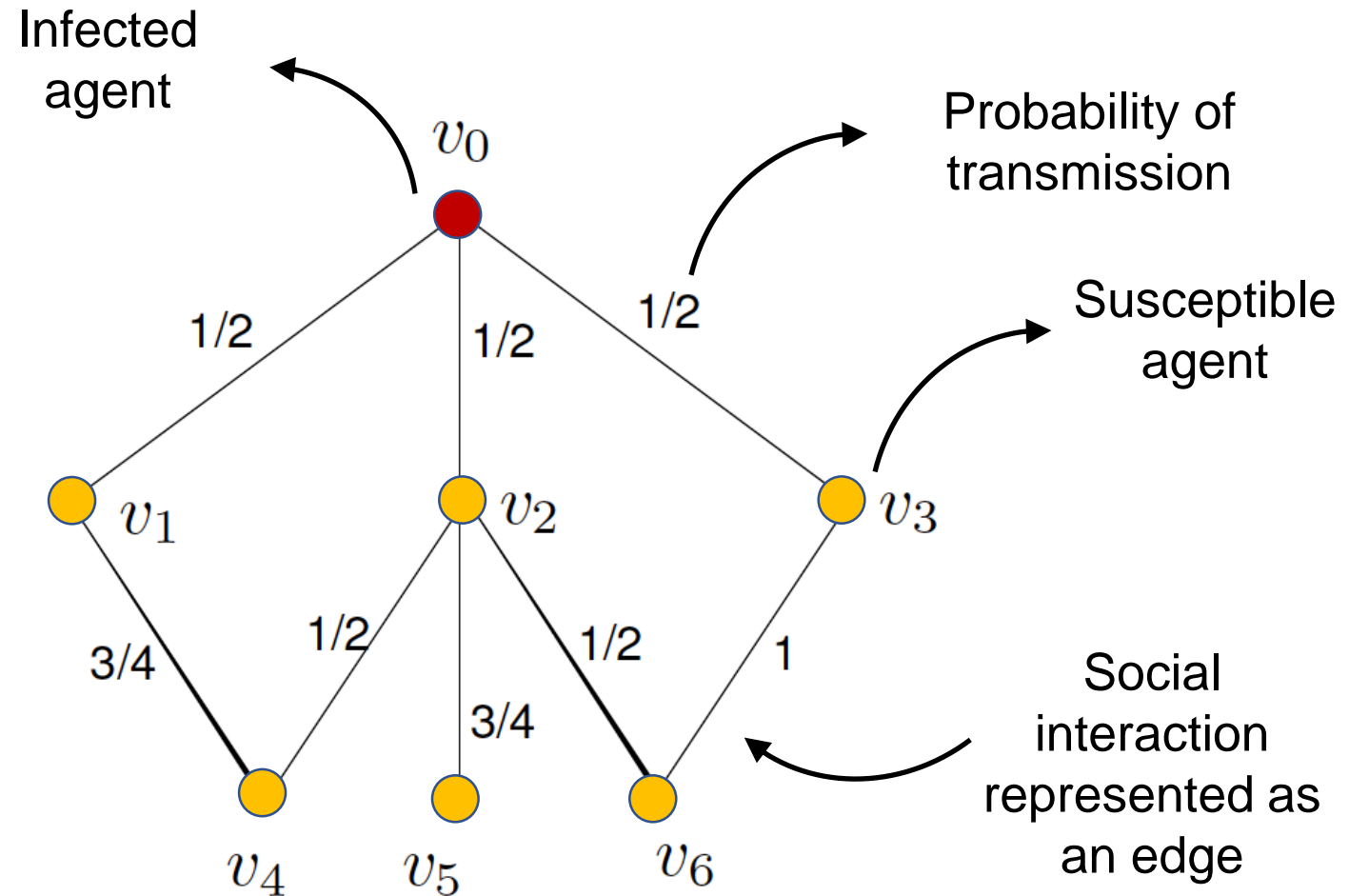
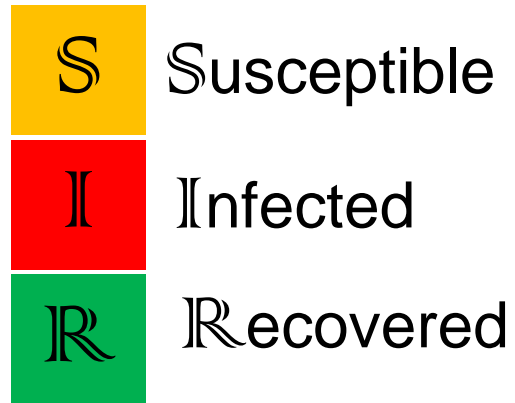
Natural immunity and secondary infections



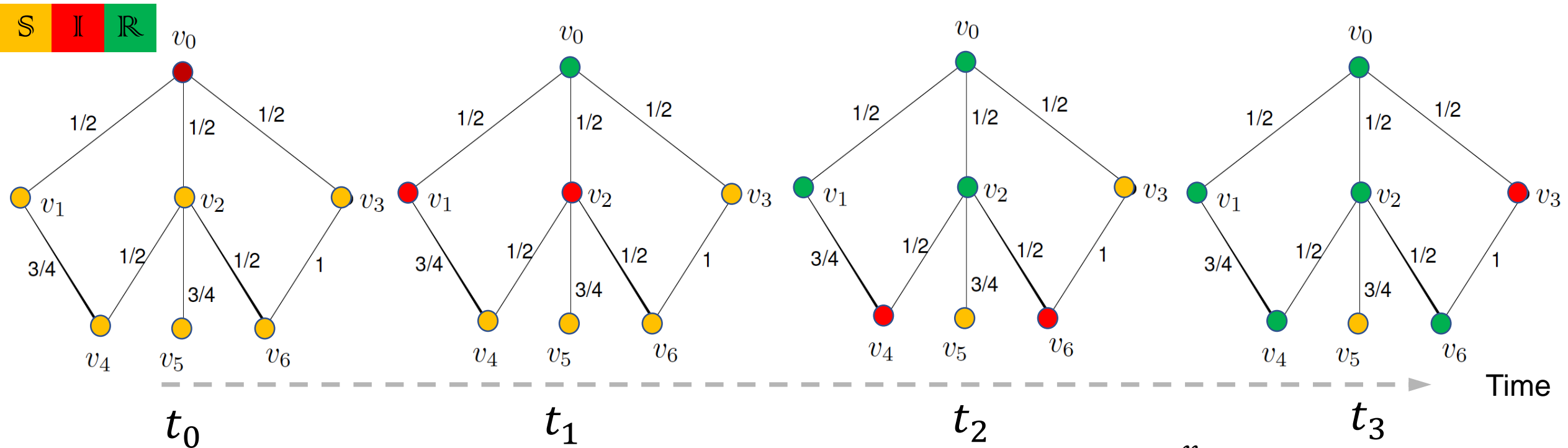
Incorporating vaccines

Directional arrows from one compartment to another represent flows
 Labels on edges represent coefficients of interactions, e.g. in the third figure, S_P interacts with I_P and I_S with interaction rates β and $\alpha\beta$ respectively.

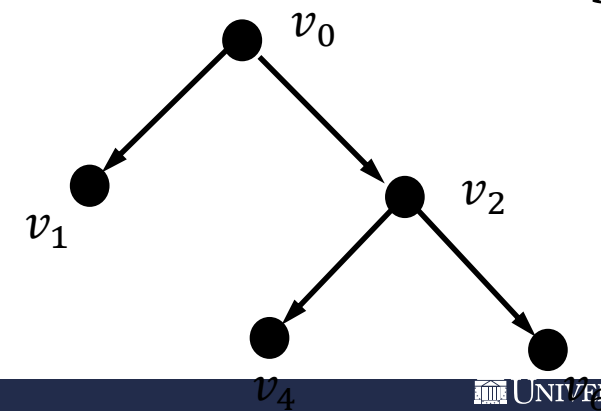
Networked epidemiology: Simple SIR model



Temporal evolution of disease spread



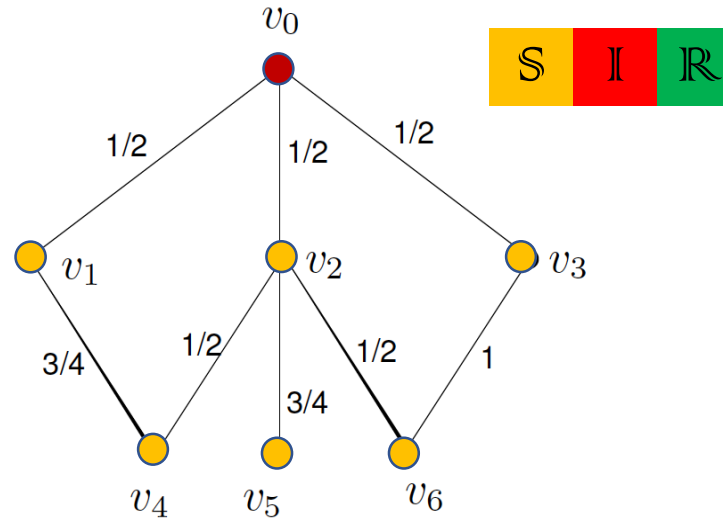
Time	Configuration
0	(I, S, S, S, S, S, S)
1	(R, I, I, S, S, S, S)
2	(R, R, R, S, I, S, I)
3	(R, R, R, I, R, S, R)
4	(R, R, R, R, R, S, R)



Simple SIR model yields a large Markov chain

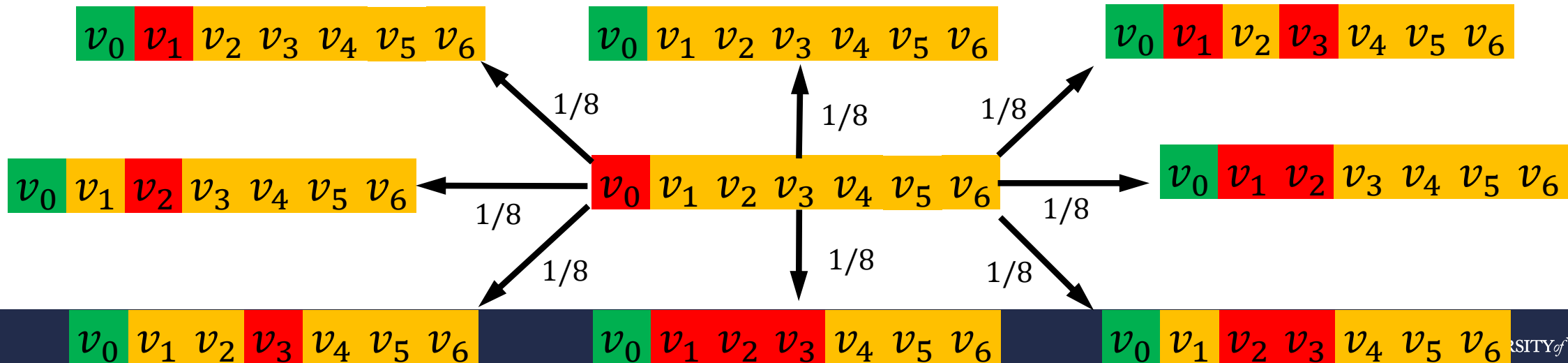
All algorithmic problems come down to analysis of this Markov chain and thus often “hard”

Temporal Dynamics represented by Markov Chain (just a fragment is depicted)



Markov chain (partial) exponentially larger than the network

A social network with n nodes & 3 disease states per nodes yields a chain of size 3^n



Computational cost of analyzing SIR dynamics

- The reachability problem is #P-hard
 - Implies that simulations are needed for understanding the dynamics
 - Even short-term reachability is hard
 - Result due to stochastic nature of the dynamical process
- *Associated Markov chain size -- astronomical in the size of the description.*
 - *Network with 10^6 nodes & (3 states: S,I,R), the chain has 3^{10^6} nodes; impossible to do naïve search*

Simulations are therefore necessary to solve this problem.

Modeling challenges for operational epidemic science

- **Challenge 1: Computational** -- most natural problems are computationally hard.
- **Challenge 2: Data** -- Sparse, noisy and lagged and incomplete --> Algorithms need to be robust to this aspect
- **Challenge 3: Near real-time** -- Decisions need to be made in near real-time, often with conflicting objectives
- **Challenge 4: Implementable interventions** -- Interventions need to be implementable in the real world
- **Challenge 5: Co-evolution** -- Decisions and epidemic co-evolves – need robust optimization framework



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).



AI+HPC Driven Real-time, Operational Epidemic Science
<https://nssac.github.io/covid-19/index>

An integrated program for real-time COVID-19 response



80+ scientists, staff & students

90+ weekly model updates



Weekly updates to state and federal agencies since February 2020

Network Systems
Science & Advanced
Computing
Biocomplexity Institute
& Initiative
University of Virginia

Estimation of COVID-19 Impact in Virginia

January 5th, 2022
(data current to Jan 2nd - 4th)
Biocomplexity Institute Technical report: TR 2022-001

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UVA COVID-19 MODEL WEEKLY UPDATE

January 7th, 2022
KEY TAKEAWAYS

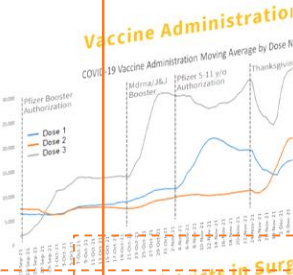
- The Omicron variant has displaced Delta and is now responsible for an estimated 94% of new cases in Virginia.
- Case rates have accelerated to unprecedented levels throughout the Commonwealth, and all 35 health districts are now in surge.
- Models project a continued sharp rise in cases for several weeks, possibly followed by an equally sharp decline.
- There is some evidence that Omicron may be less severe than Delta, but the explosion of new cases is still expected to put an enormous burden on communities and the healthcare system.
- The sheer number of new cases may overwhelm testing capacities and drive down the case detection rate. As such, case rates may not be as reliable a marker of epidemic trends as they once were.

152 per Average Daily Week Ending
673 per Omicron Scenarios Forecast Avg. Cases, Week on Jan. 23, 2022
6,891 per Average Daily Jan. 2, 2021
18,798 per Average Daily Jan. 2, 2021

KEY FIGURES

Reproduction Rate (Based on Confirmation Date)

Region	R ₀ Jan. 3rd	Change vs Previous
Statewide	1.158	0.042
Central	1.170	0.111
Eastern	1.213	0.141
Far SW	1.114	0.195
Near SW	1.225	0.302
Northern	1.138	-0.043
Northwest	1.213	0.217



Growth Trajectories: All 35 Health Districts in Surge

Status	# Districts (prev report)
Declining	0 (5)
Plateau	0 (0)
Slow Growth	0 (9)
In Surge	35 (21)

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UVA COVID-19 MODEL WEEKLY UPDATE

THE MODEL

The UVA COVID-19 Model and these weekly results are provided by the UVA Biocomplexity Institute, which has over 20 years of experience crafting and analyzing infectious disease models. It is a county-level Susceptible, Exposed, Infected, Recovered (SEIR) model designed to evaluate policy options and provide projections of future cases based on the current course of the pandemic. The Institute is also able to model alternative scenarios to estimate the impact of changing health behaviors and state policy.

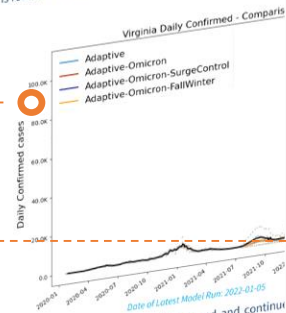
THE SCENARIOS

Updated: The model uses various scenarios to explore the path the pandemic is likely to take under different "Adaptive" scenarios. The model continues to track the current course of the pandemic assuming that the Delta dominant. Though genomic surveillance data is still pending, CDC estimates suggest that the Omicron displaced it. This model scenario is retained for comparison purposes but will likely be retired in the coming weeks. All other model scenarios are based on the immune escape profiles of the new Omicron strain. This figure assumes that Omicron is as transmissible as Delta, but with an added immune escape of 80%. This figure from 30% since the last model run. The "Adaptive-Omicron-SurgeControl" scenario shows the likely impact of mitigation efforts (masking, social distancing, testing and isolating, etc.) on the impending Omicron surge. The "Adaptive-Omicron-FallWinter" scenario shows a drop in transmission rates starting next week. In this scenario, the transmission rates start next week and then falling by employing a 25% reduction in the entire 2020 holiday season and projects them forward. This scenario captures the transmission drivers of the entire 2020 holiday season and projects them forward. In this scenario, the transmission rates from January 2021 to February 2022 are manually set to reflect the sharply rising and then falling uptake continues in each county until this value is reached and 40% of vaccinated individuals will receive a second dose.

MODEL RESULTS

Updated: The Delta-dominant "Adaptive" scenario (light blue) shows a continued gradual rise in cases, peaking in mid-January at around 95,000 cases per week. Given Omicron's displacement of Delta, this seems overly optimistic.

All three Omicron scenarios are largely identical in the short term. They project a continued sharp rise in cases, peaking around 350,000-400,000 cases per week in the second half of January. The difference between these three scenarios is in the decline after the peak. The "Omicron" scenario (maroon) forecasts a gradual decline into April. The "SurgeControl" scenario (purple) shows a steeper decline into April. The "FallWinter" scenario (orange) shows a drop off matching the one seen last winter, reaching a rate of fewer than 30,000 weekly cases by the middle of March.



Please do your part to stop the spread and continue prevention, including indoor masking, social distancing, and get vaccinated and boosted with

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COVID-19 is virus, and the mix changes as we learn it

UVA COVID-19 MODEL WEEKLY UPDATE

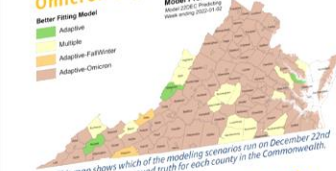
ANOTHER WINTER STORM

This week Virginia was hit by a winter storm that dumped up to 14" of snow on some parts of the Commonwealth. The damage to power lines and effects on highway traffic were substantial. Yet it was a bit of a surprise to some given the preceding week of unseasonably warm weather. Virginia is now facing a different kind of winter storm, and one that won't melt away so quickly. After a relatively calm November and early December, case rates suddenly surged following the introduction of the Omicron variant (B.1.1.529). This was likely compounded by cold and dry winter weather, and holiday travel and gatherings. Models now forecast a repeat of last year's winter surge, with another peak in late January. Unfortunately, Omicron's extensive immune escape may allow this year's surge to dwarf those of 2021.



A satellite view of Tuesday's Winter Storm. Source: Joshua Stevens of the NASA Earth Observatory with MODIS, EOSDIS LANCE and GIBS Worldview.

Omicron Supplants Delta



This map shows which of the modeling scenarios ran on December 22nd was closest to the ground truth for each county in the Commonwealth.

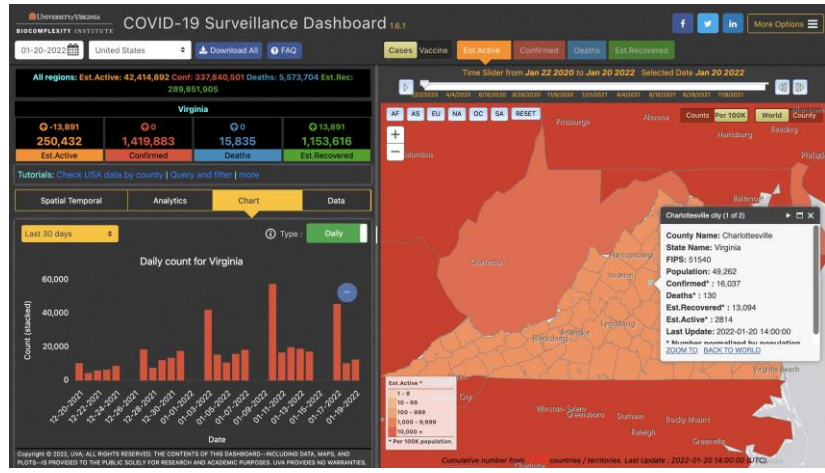
The Good, the Bad, and the Ugly

There is some good news: Preliminary evidence suggests that Omicron may be less virulent than Delta and earlier variants. This may be the result of the variant's weaker ability to attack the lungs. Moreover, while the variant seems adept at dodging antibodies, and can cause breakthrough cases and reinfections, T-cell response remains strong. This suggests that vaccinations should still be quite protective against severe disease and hospitalization. The bad news is that the virus is potentially 70x better at infecting airways than Delta, and with its enhanced immune escape, is causing extreme spikes in case rates across the United States. Though milder than Delta, Omicron is far from harmless, and far more than "just a cold". It is still hospitalizing substantial numbers of patients, and still carries the risk of long COVID. The ugly bit is that Virginia's hospitals will still be hit hard by the Omicron surge, despite seeming less virulent than Delta, it is causing so many more cases than Delta did, that models forecast a deluge of hospitalizations far exceeding those of last winter. Fortunately, each of us has the tools available at preventing infection and severe disease by Omicron. Boosters appear to be effective at preventing infection and severe disease by Omicron. The advice for preventing Omicron remains the same as with other COVID-19 variants: Continue to practice good prevention, including indoor masking, social distancing, and self-isolating when sick; and get vaccinated and boosted as soon as eligible.

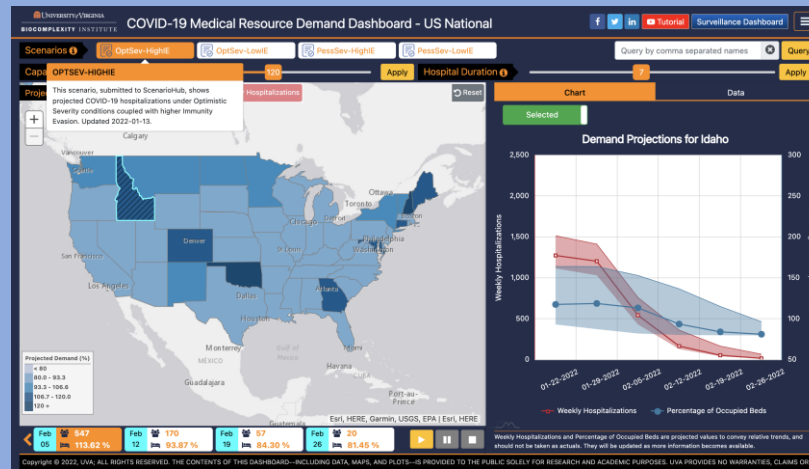
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- Literature surveys
- Situation assessments
- Model projections
- Narrative summaries

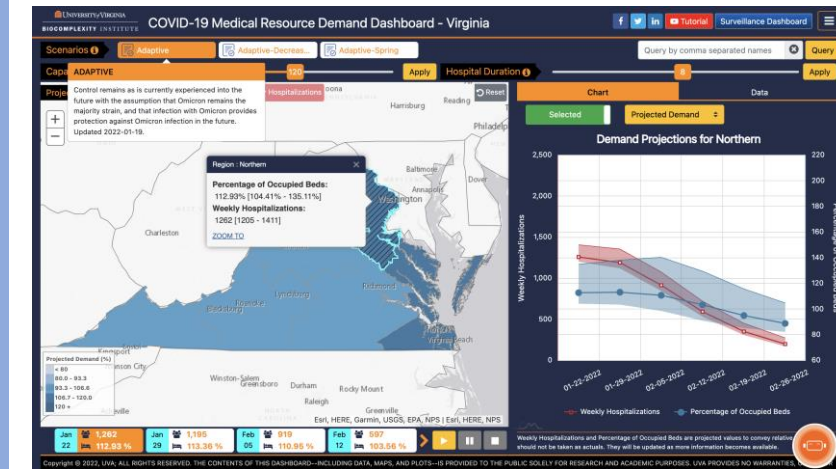
COVID-19 Surveillance



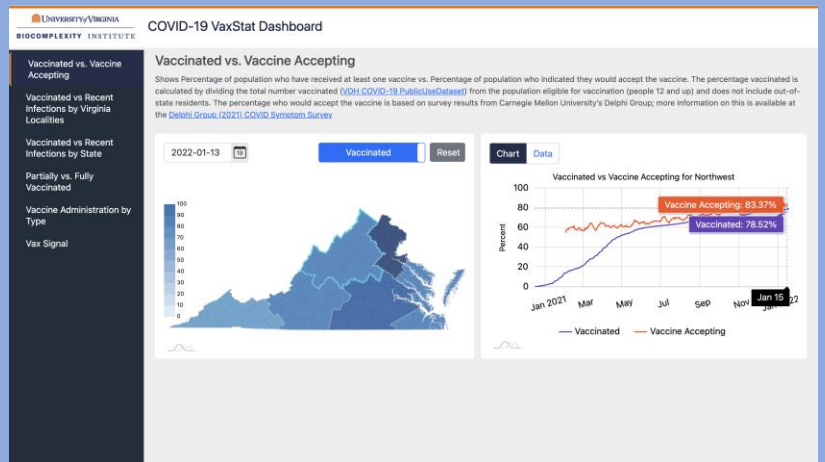
US Medical Resource Demand



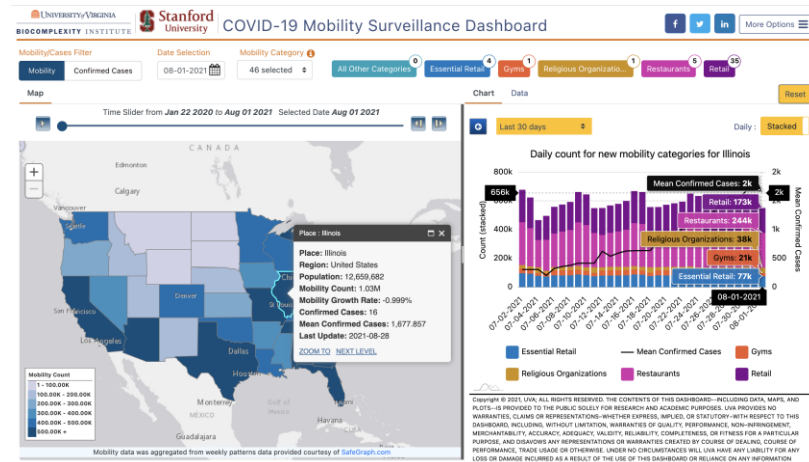
VA Medical Resource Demand



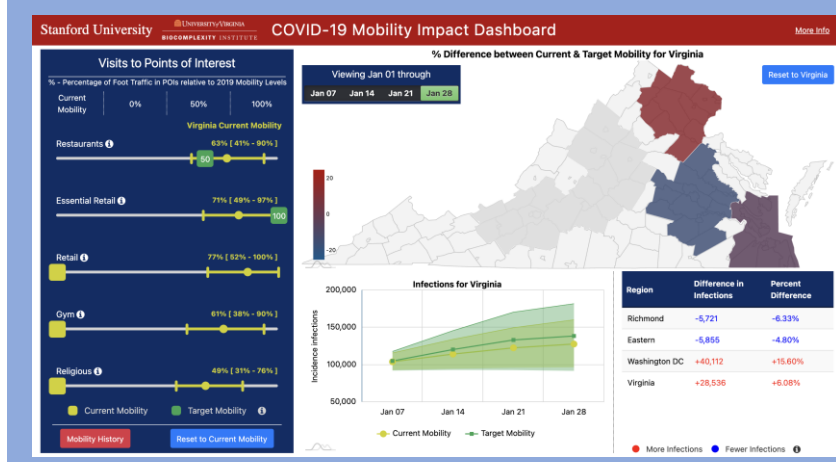
Vaccine Status



COVID-19 Mobility Surveillance



COVID-19 Mobility Impact



Decision support dashboards
<https://nssac.github.io/covid-19/index>

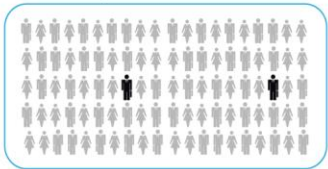
Overall approach

Component 1: Digital twin of US social contact

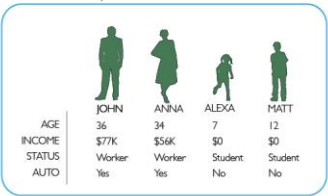
POPULATION INFORMATION

- Census data (e.g., PUMS)
- Application specific data

Iterative
proportional
fitting



Household
grouping

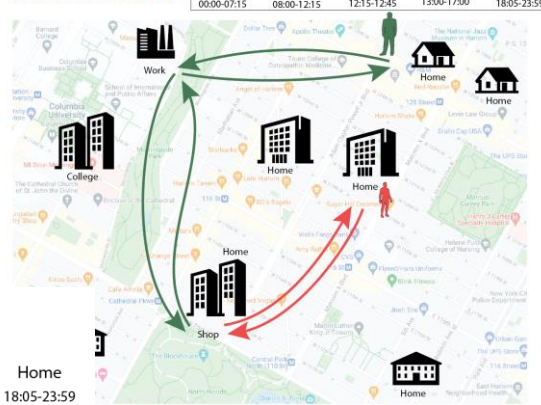


Base population partitioned
into households/groups

LOCATION CONSTRUCTION



LOCATION ASSIGNMENT

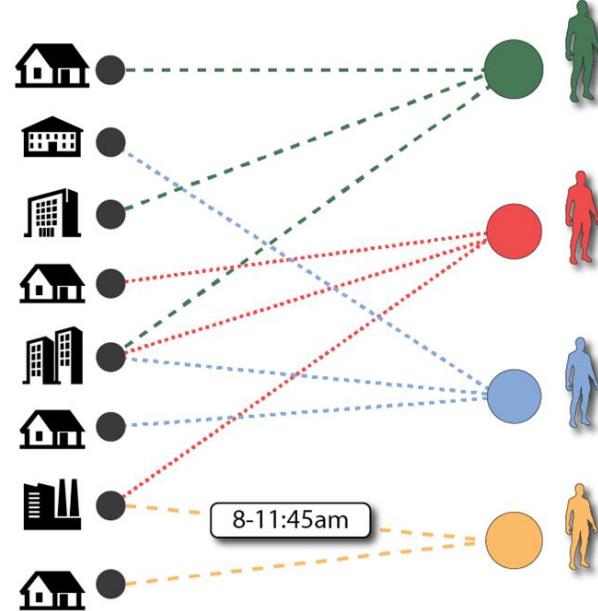


NETWORK CONSTRUCTIONS

Locations



Persons



People-location network

REPRESENTED SCALES



BEHAVIOR EXAMPLES

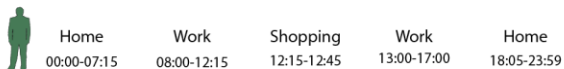


INTERACTIONS ACROSS SCALES



Social contact network

ACTIVITY SEQUENCE ASSIGNMENT



Digital twin captures heterogeneous spatially explicit, multi-scale, multi-theory, multi-level social contact network representations

Component 2: EpiHiper -- a parallel agent-based socio-epidemic simulator



Inputs: disease model + Social contact network from Digital Twin



Agent-based discrete time/event simulation model



Contact network partitioned onto MPI ranks



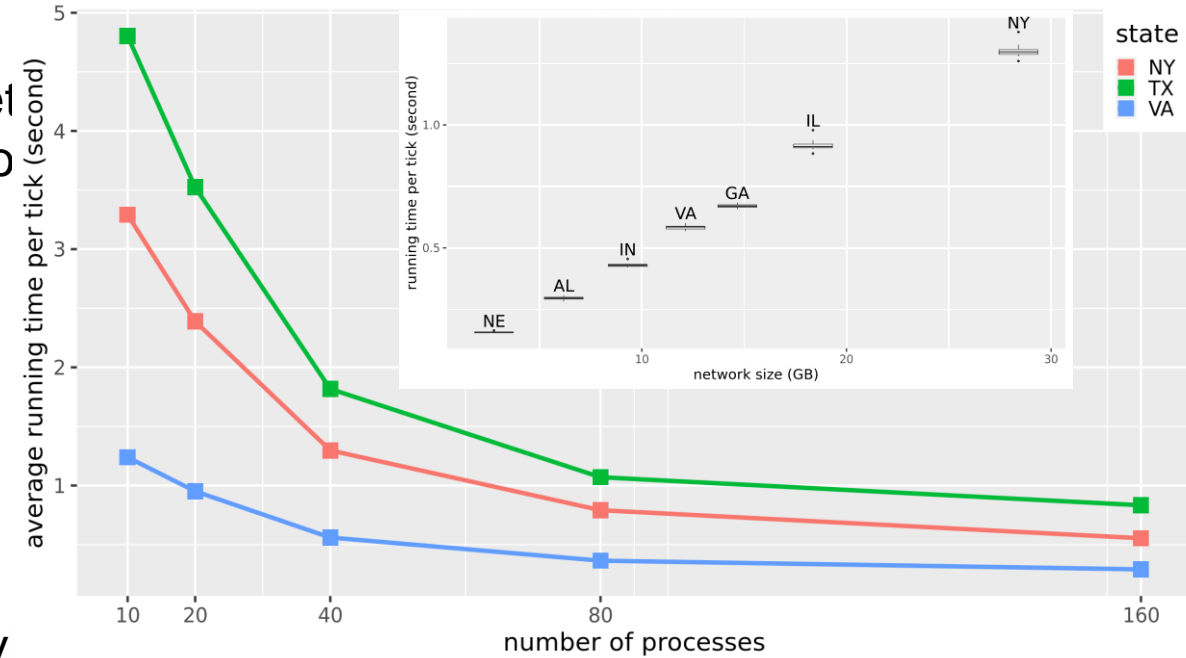
Distributed memory program written in C++/MPI



Custom domain-specific language for programming NPI scenarios

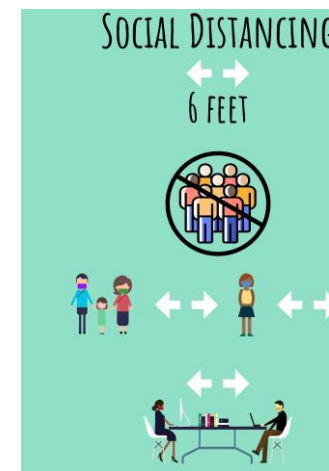


Shared inputs served via PostgreSQL database



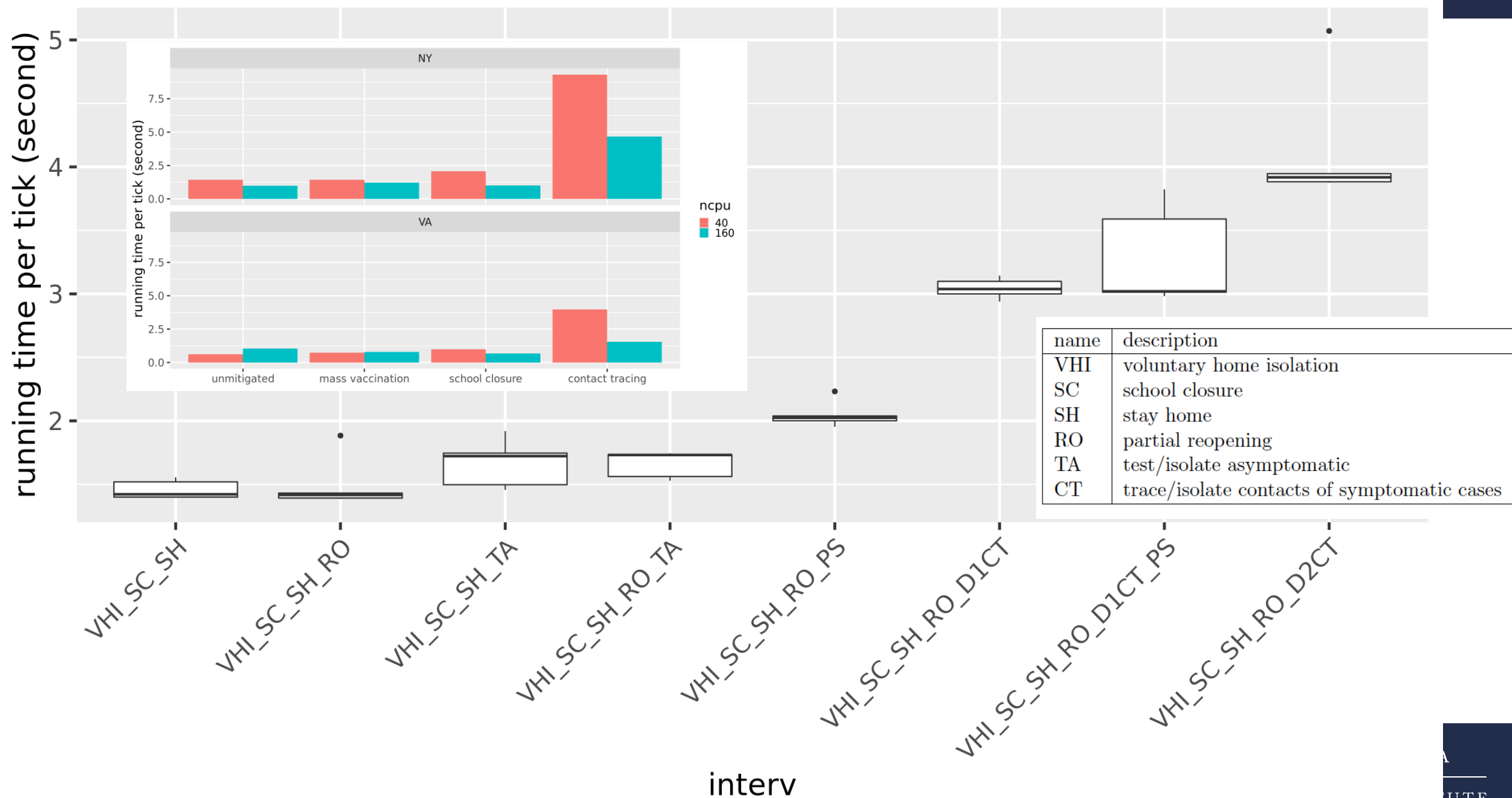
Interventions

- Pharmaceutical (PI) vs non-pharmaceutical (NPI)
 - Vaccination, Antivirals
 - Isolation, Sequestration, Quarantine, social-distance
- Public health vs individual
 - Work/school closure, Wearing a mask, self isolation
- Pre-specified vs online
- Static (independent of simulation outcome) vs dynamic (dependent on simulation progress)
- Targeted vs un-targeted

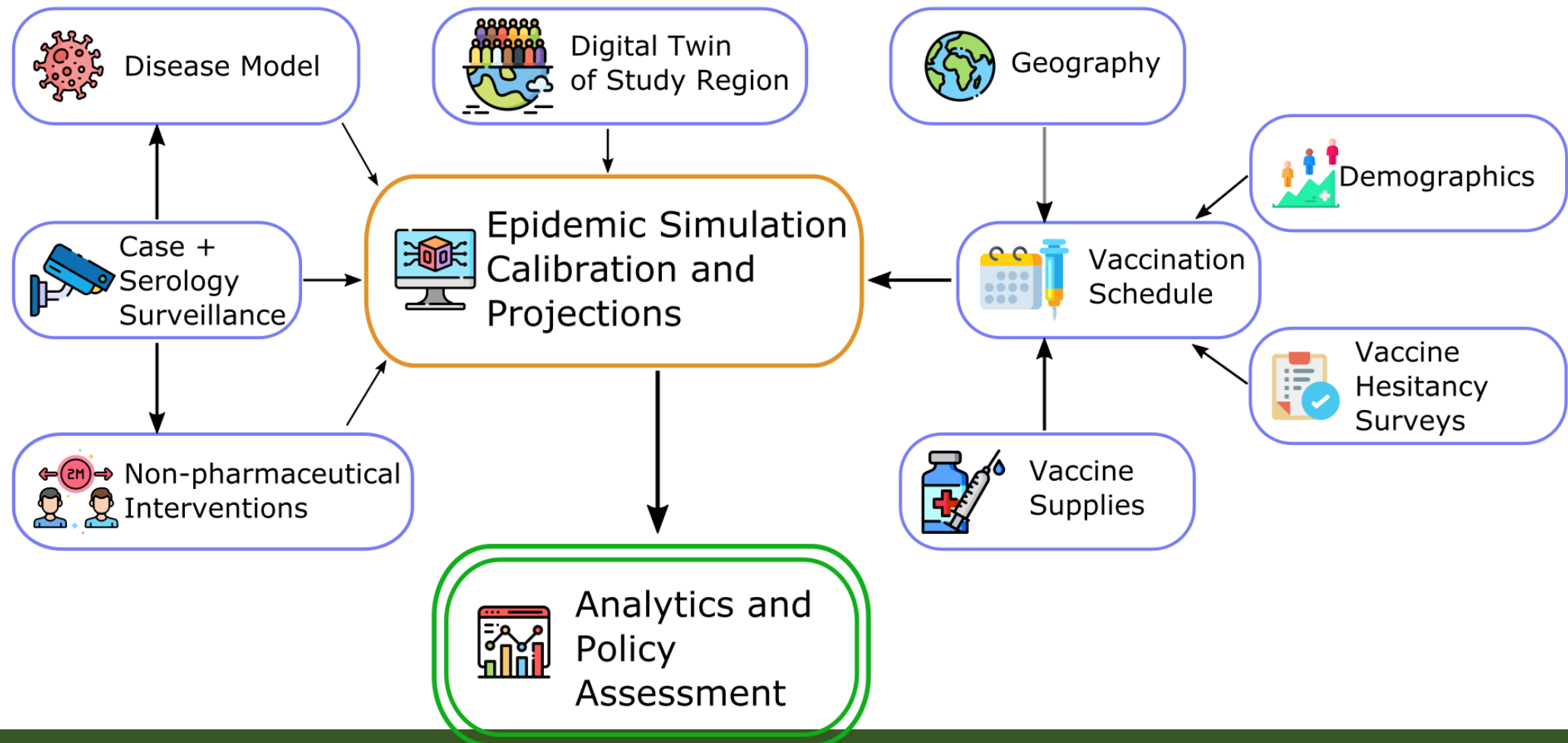


if **conditions (triggers)** are satisfied.
apply **action** (with *parameters*) to
subnetwork (chosen with
constraints)

Interventions are expensive



Component 3: Live digital twin (DT)



Bringing the digital twin to life: Contextualize the DT with current ground conditions

Risk of importation
of disease to various
parts of the world

Forecasting the
future course of the
pandemic with and
without
interventions

Resource
augmentation, e.g.
building field
hospitals and
resource sharing,
e.g. ventilators

Analytical workflows for COVID-19

Counterfactual
analysis to study
how the pandemic
will evolve under
various scenarios

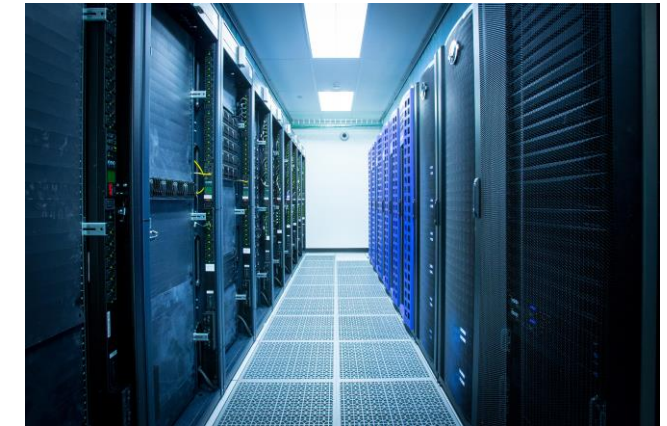
Projecting the
healthcare demands
including PPE,
ventilators, beds

Economic impact
analysis:
cost/benefit analysis
of interventions

Integrated workflow orchestration across two supercomputers



20,000 cores



2,000 cores

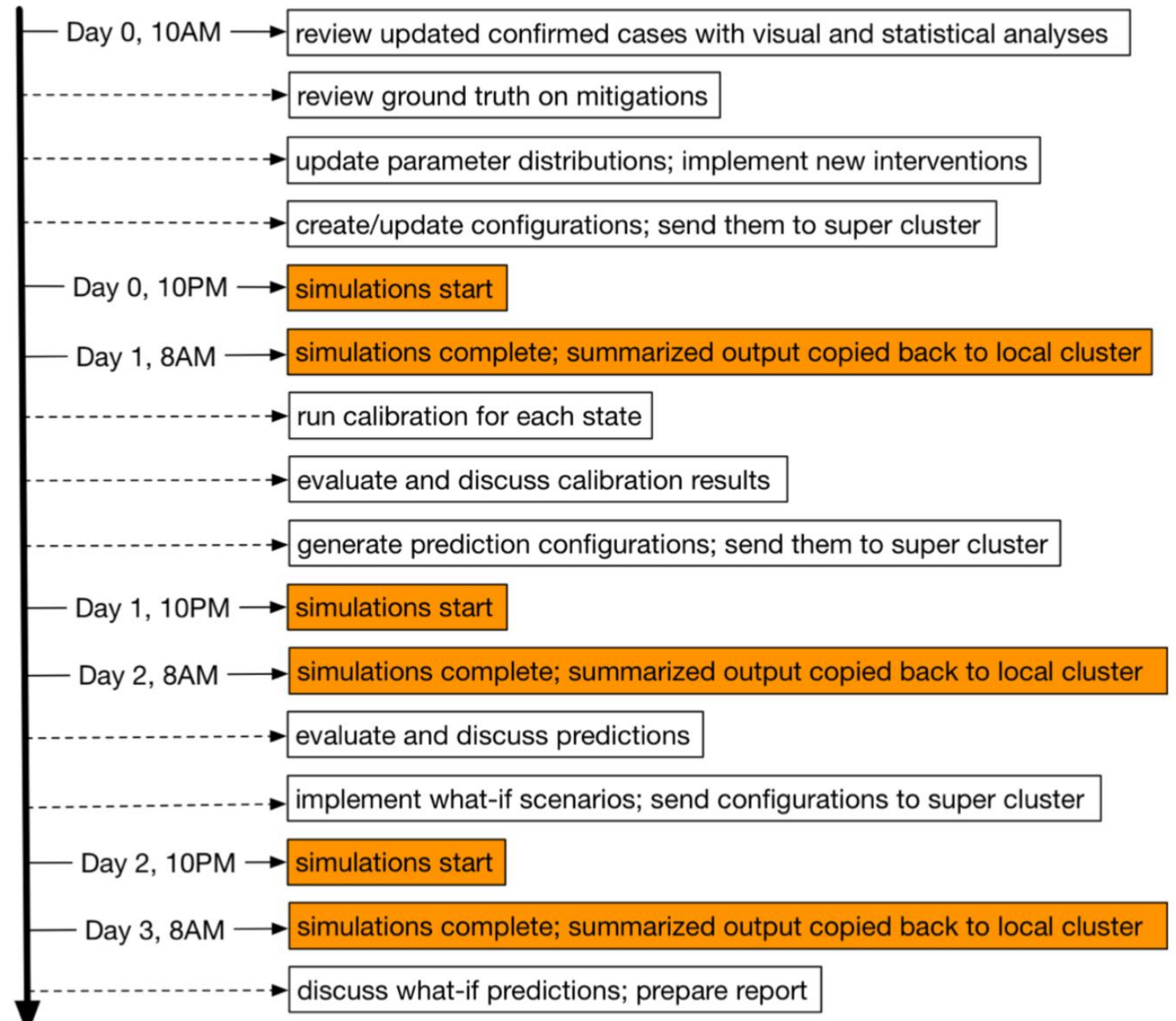
Incredible support by UVA Computing, PSC and XSEDE: Rick, Shawn Brown, John Towns and their team made this happen and provided unprecedented access and real-time support

	Remote Cluster Bridges@PSC	Home Cluster Rivanna@UVA
#Allocated nodes	720	50
#CPUs/node	2	2
#Cores/CPU	14	20
RAM/node	128GB (DDR4)	384GB (DDR4)
CPU	Intel Haswell E5-2695 v3	Intel Xeon Gold 6148
Network	Intel Omni path-1	Mellanox ConnectX-5
Filesystem	Lustre	Lustre

HPC-Enabled workflows for real-Time epidemiology

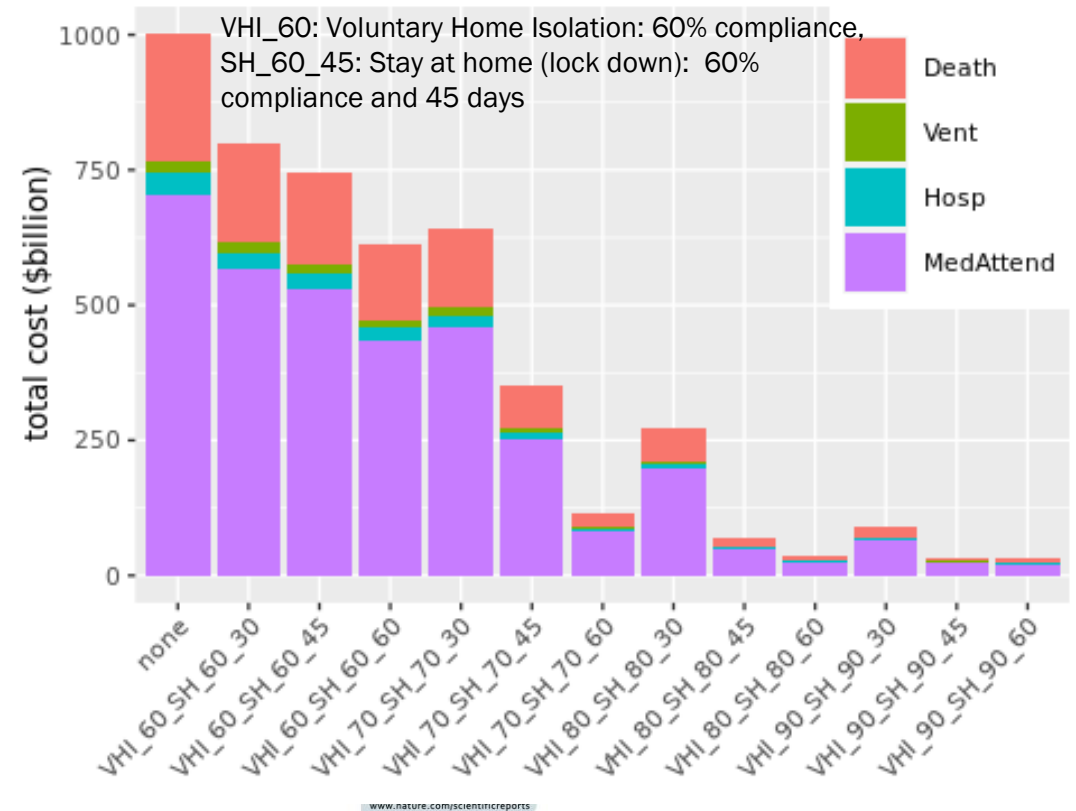
During March- November 2020

- Typically, per night, the pipeline runs 5,000-17,900 regional or national simulations
- Network with 300 million nodes and 7.9 billion edges partitioned across all 50 states
- The simulations yield ensemble models for prediction of epidemic incidence curves at the US county level (3243 counties).



Computing medical costs

- Objective:
 - Analyze economic impact of infections and NPI's (Medical costs)
- Study settings:
 - calibrated COVID-19 disease model
 - NPI's with parameter sweep on compliance and duration
 - medical costs due to hospitalizations and deaths
 - GDP reduction due to cascading effects between sectors from workforce interruptions not computed
- Findings:
 - Total medical cost decreases with NPI compliance and duration.
 - NPI's have significant impact on Medical costs



scientific reports

OPEN Epidemiological and economic impact of COVID-19 in the US

Jiangzhuo Chen¹, Anil Vullikanti^{2,3}, Joost Santos⁴, Srinivas Venkatramanan¹, Stefan Hoops⁵, Henning Mortveit^{1,4}, Bryan Lewis², Wen You⁶, Stephen Eubank^{1,2}, Madhav Marathe^{1,2}, Chris Barrett^{1,2} & Achia Marathe^{1,2}

This research measures the epidemiological and economic impact of COVID-19 spread in the US under different mitigation scenarios, comprising of non-pharmaceutical interventions. A detailed disease model of COVID-19 is combined with a model of the US economy to estimate the direct impact of labor supply shock to each sector arising from morbidity, mortality, and lockdown, as well as the indirect impact caused by the interdependencies between sectors. During a lockdown, estimates of jobs that are workable from home in each sector are used to modify the shock to labor supply. Results show trade-offs between economic losses, and lives saved and infections averted are non-linear in compliance to social distancing and the duration of the lockdown. Sectors that are worst hit are not the labor-intensive sectors such as the Agriculture sector and the Construction sector, but the ones with high valued jobs such as the Professional Services, even after the teleworkability of jobs is accounted for. Additionally, the findings show that a low compliance to interventions can be overcome by a longer shutdown period and vice versa to arrive at similar epidemiological impact but their net effect on economic loss depends on the interplay between the marginal gains from averting infections and deaths, versus the marginal loss from having healthy workers stay at home during the shutdown.

www.nature.com/scientificreports

scientific reports

OPEN Medical costs of keeping the US economy open during COVID-19

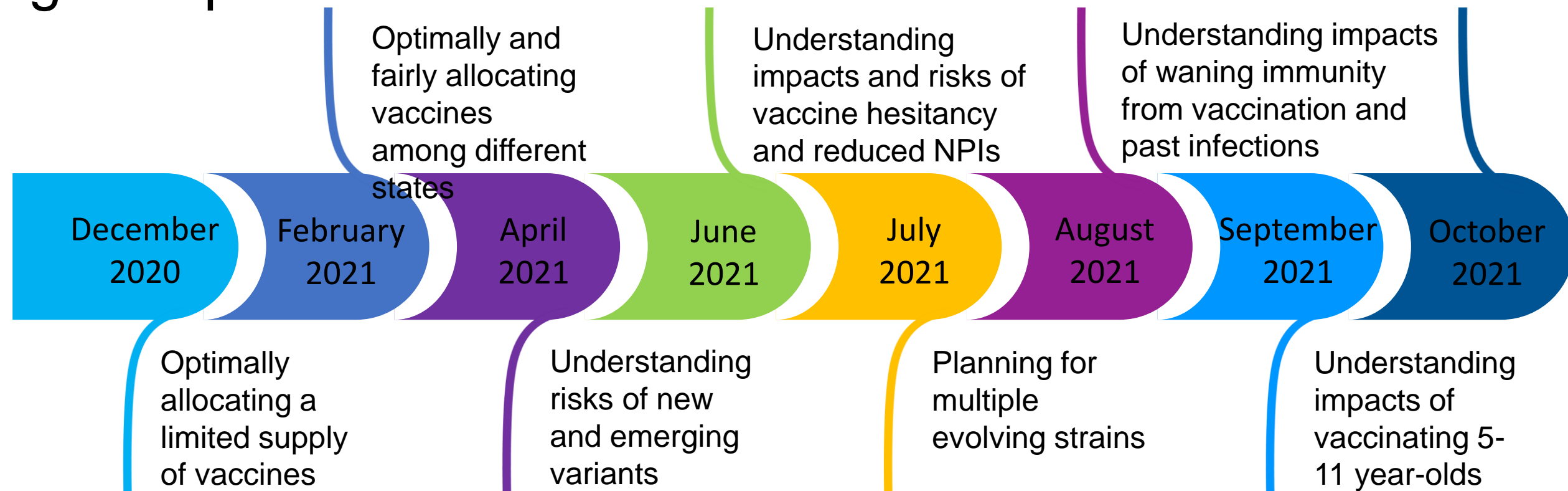
Jiangzhuo Chen¹, Anil Vullikanti^{2,3}, Stefan Hoops⁵, Henning Mortveit^{1,4}, Bryan Lewis², Srinivas Venkatramanan¹, Wen You⁶, Stephen Eubank^{1,2}, Madhav Marathe^{1,2}, Chris Barrett^{1,2} & Achia Marathe^{1,2}

We use an individual based model and national level epidemic simulations to estimate the medical costs of keeping the US economy open during COVID-19 pandemic under different counterfactual scenarios. We model an unmitigated scenario and 12 mitigation scenarios which differ in compliance behavior to social distancing strategies and in the duration of the stay-home order. Under each scenario we estimate the number of people who are likely to get infected and require medical attention, hospitalization, and ventilators. Given the per capita medical cost for each of these health states, we compute the total medical costs for each scenario and show the tradeoffs between deaths, costs, infections, compliance and the duration of stay-home order. We also consider the hospital bed capacity of each Hospital Referral Region (HRR) in the US to estimate the deficit in beds each HRR will likely encounter given the demand for hospital beds. We consider a case where HRRs share hospital beds among the neighboring HRRs during a surge in demand beyond the available beds and the impact it has in controlling additional deaths.

Chen, J., Vullikanti, A., Hoops, S., Mortveit, H., Lewis, B., Venkatramanan, S., You, W., Eubank, S., Marathe, M., Barrett, C. and Marathe, A., 2020. Medical costs of keeping the US economy open during COVID-19. *Scientific reports*, 10(1), pp.1-10.

Supporting the scenario modeling hub

Problem: Real time scenario projections in an evolving global pandemic



The scenario projection problem: Given the current conditions on the ground, and a set of possible future scenarios, the goal is to assess the likelihood of epidemiological outcomes for each of these scenarios by analyzing the output of our simulations.

Assessing the impact of waning immunity (Example)

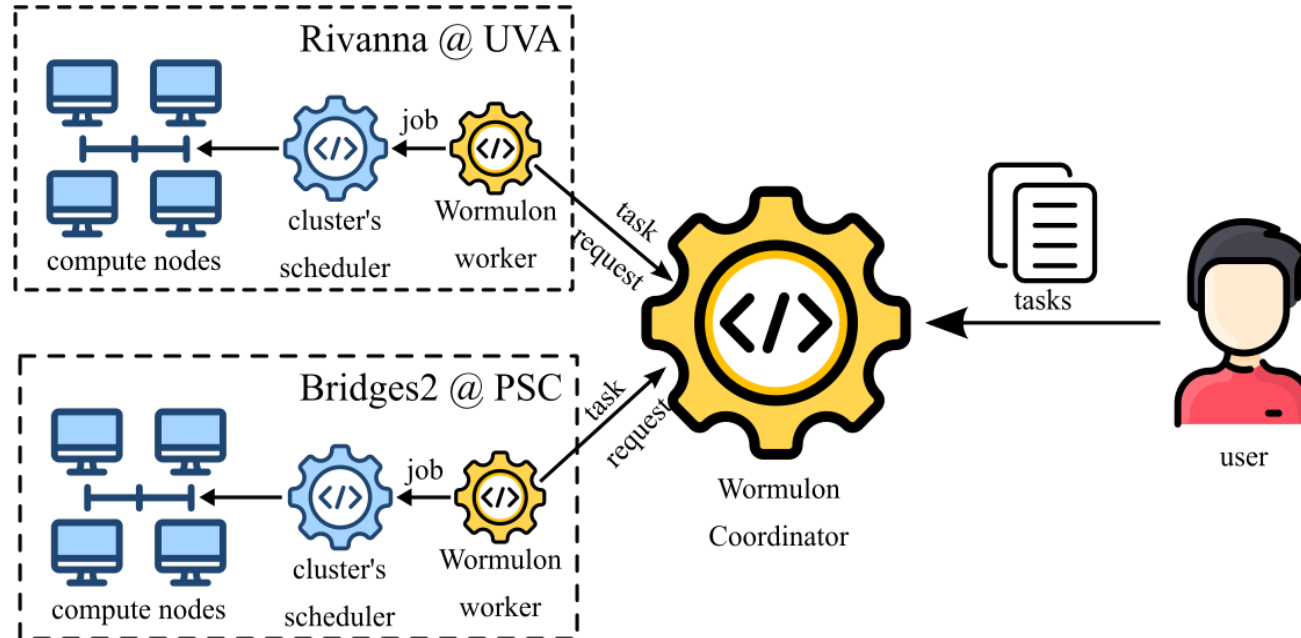


Scenario projections from 9 teams are harmonized to assist decision makers with COVID-related planning for the next 3-6 months

Each model projects six different targets (variables) for the US at state- or county-level resolution

<p>Round 12</p>	<p>Higher immune escape: 80% of previously immune are susceptible to infection</p>	<p>Lower immune escape: 50% of previously immune are susceptible to infection</p>
<p>Lower severity: 70% reduction in severity of Omicron infection, relative to Delta (all-age risk of hospitalization and death times 0.3) among all immune classes.</p>	<p>Scenario A Optimistic severity, High immune escape</p>	<p>Scenario B Optimistic severity, Low immune escape</p>
<p>Higher severity: 30% reduction in severity of Omicron infection, relative to Delta (all-age risk of hospitalization and death times 0.7) among all immune classes.</p>	<p>Scenario C Pessimistic severity, High immune escape</p>	<p>Scenario D Pessimistic severity, Low immune escape</p>

Hybrid HPC pipeline: orchestrating two supercomputers



- Leverages HPC schedulers at HPC clusters & runs on modern secure clusters
- Supports task dependency and dynamic task creation
- Supports task semantic-aware fault detection and retries
- Supports disparate HPC site-specific configurations
- Coordinator-Worker architecture: Single coordinator & a cluster worker per HPC cluster

Data intensive, real-time, end-to-end HPC-workflows

Inputs

3100 US counties
500 days
confirmed case count data

~20GB synthetic population
person, household, location, and activities data

300 million nodes and 12 Billion edges

Simulations

~10200 simulation instances
factorial design

2550 simulation instances
calibration

33 hours
9000 cores
spread over two machines

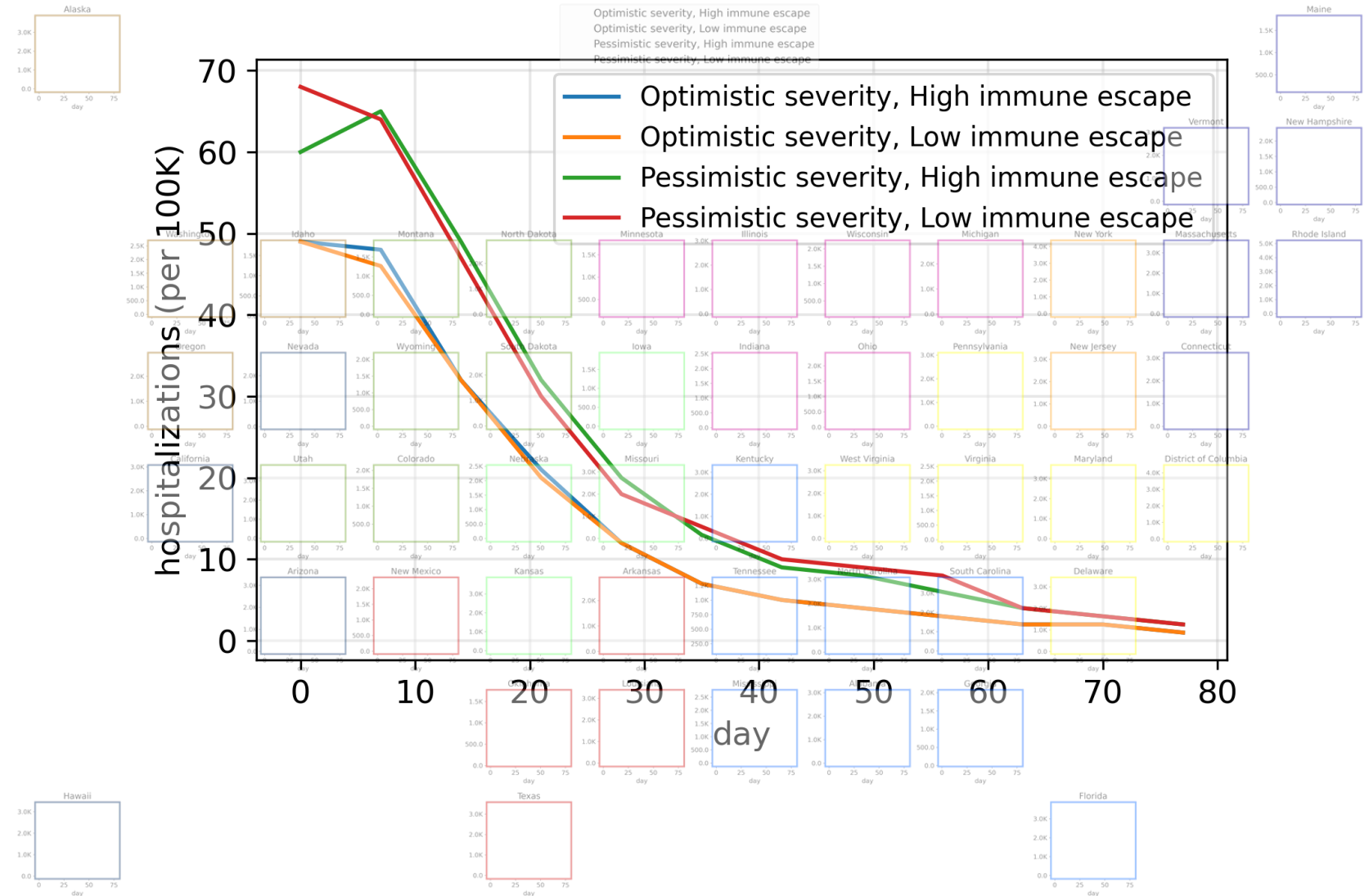
Outputs

~1.5B entries, ~4GB aggregate output data
250 days, 200 health states, 3 counts

~4TB individual-level output data
multi-million state transitions = multi-billion entries

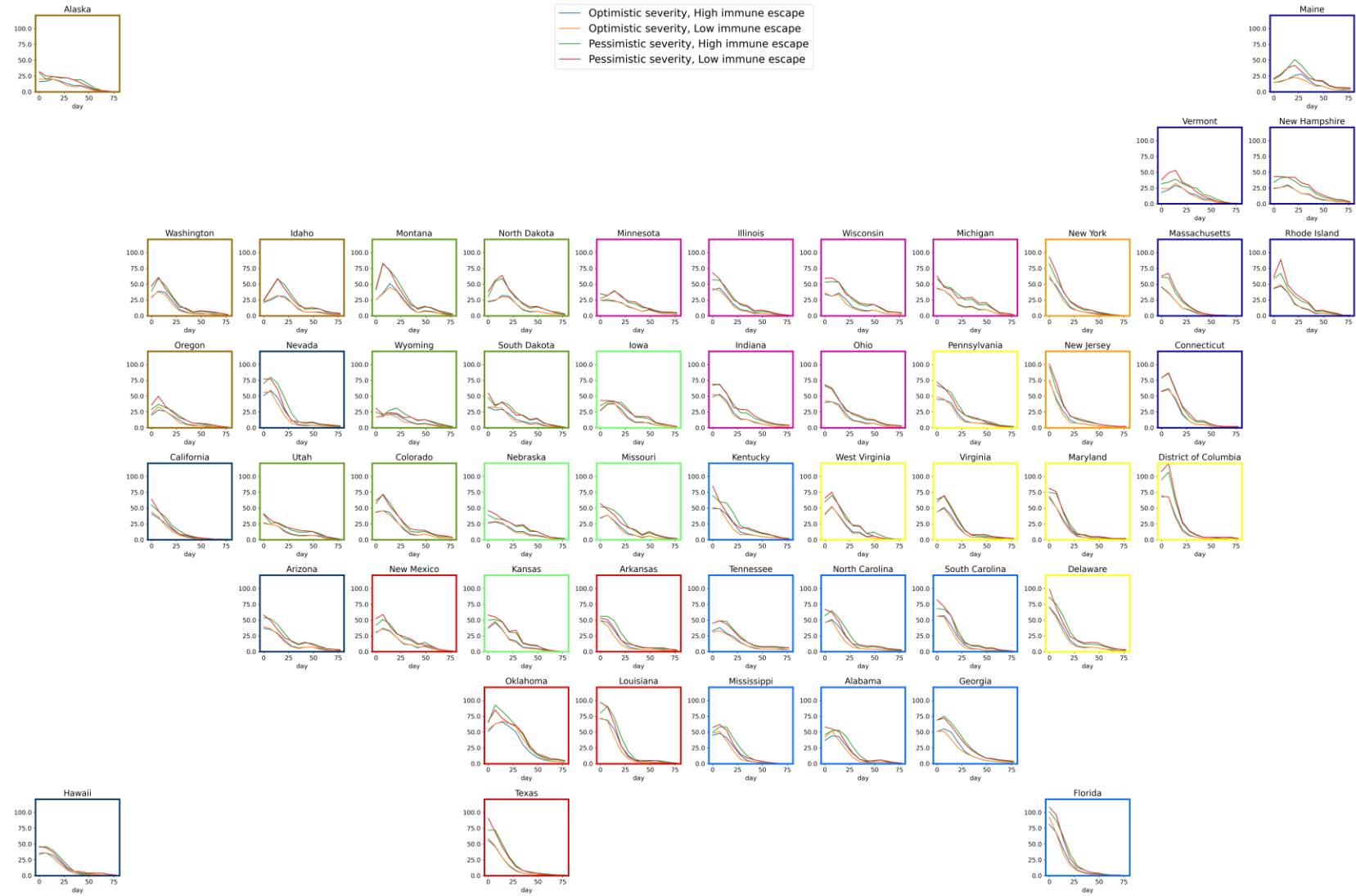
Spatio-temporal variability of the projection: hospitalizations in US

- Pessimistic severity scenarios result in larger number of hospitalizations
- Effect of immune escape is relatively small
- Hospitalizations rapidly decrease next month in all scenarios



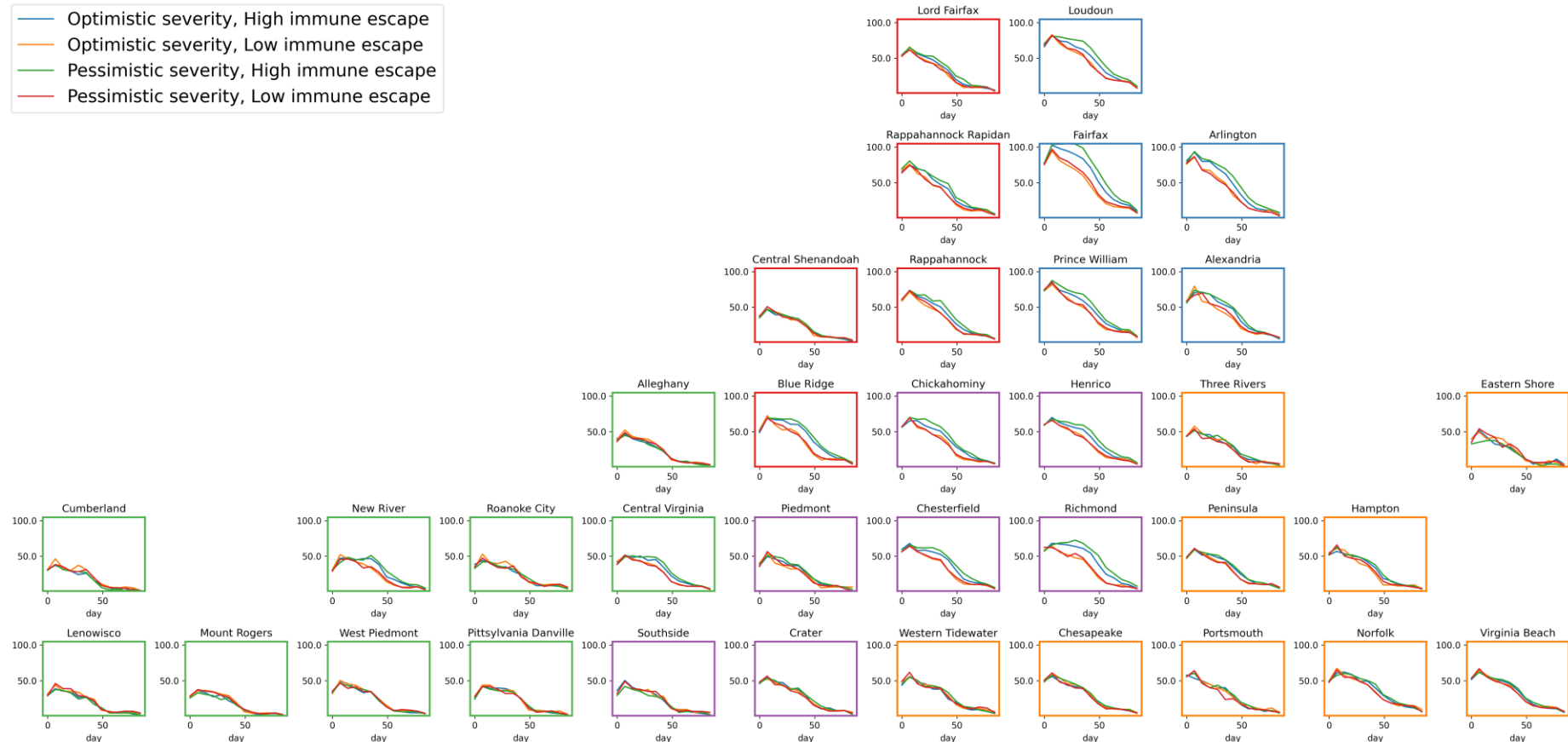
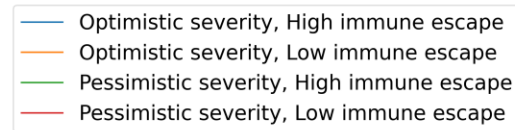
Spatio-temporal variability of the projection: hospitalizations in US

- Pessimistic severity scenarios result in larger numbers of hospitalizations
- Hospitalizations rapidly decrease in next month in all scenarios
- Significant differences between states



Spatio-temporal variability of the projection: hospitalizations in Virginia health districts

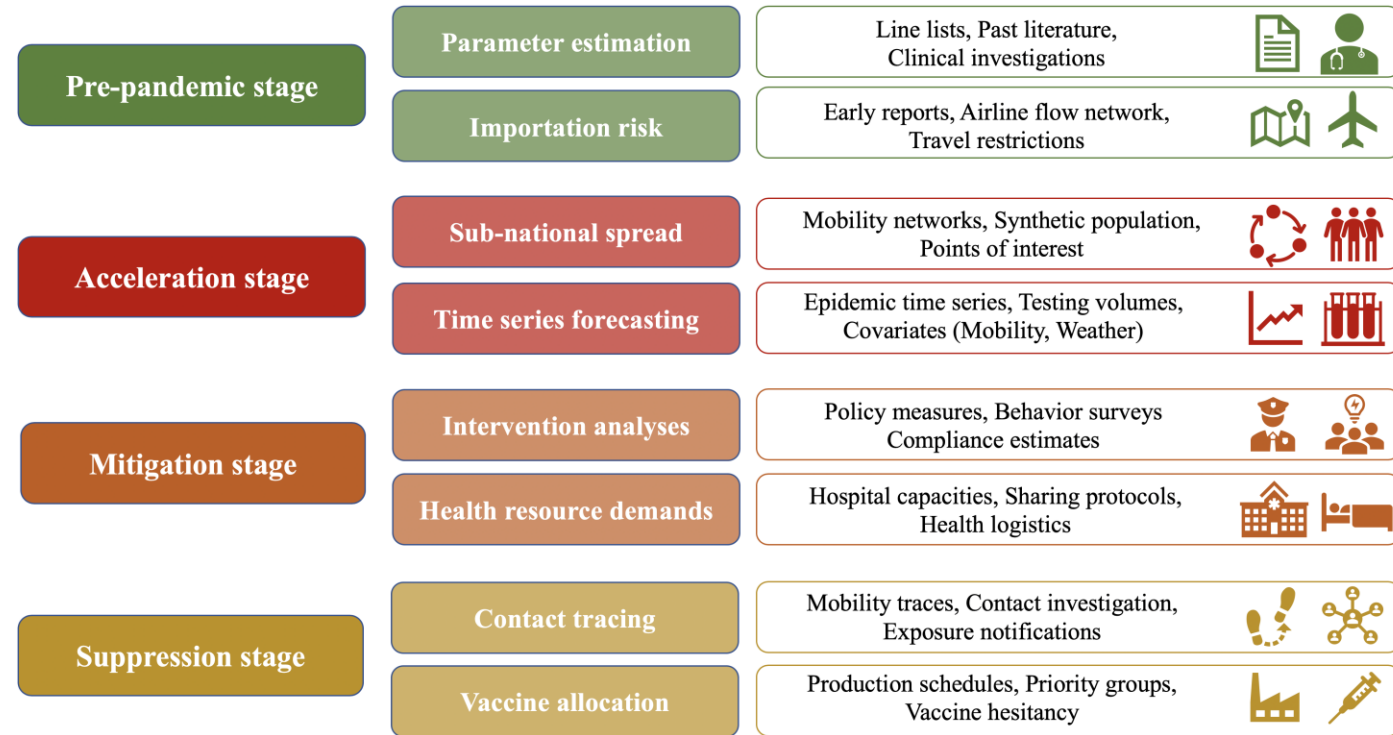
- Hospitalizations peak in January 2022 in all districts, then rapidly decrease next month in all scenarios
- Significant differences between districts
- Higher number of hospitalizations (normalized by population) in Northern VA



Challenges for Data Scientists and AI

Data Challenge

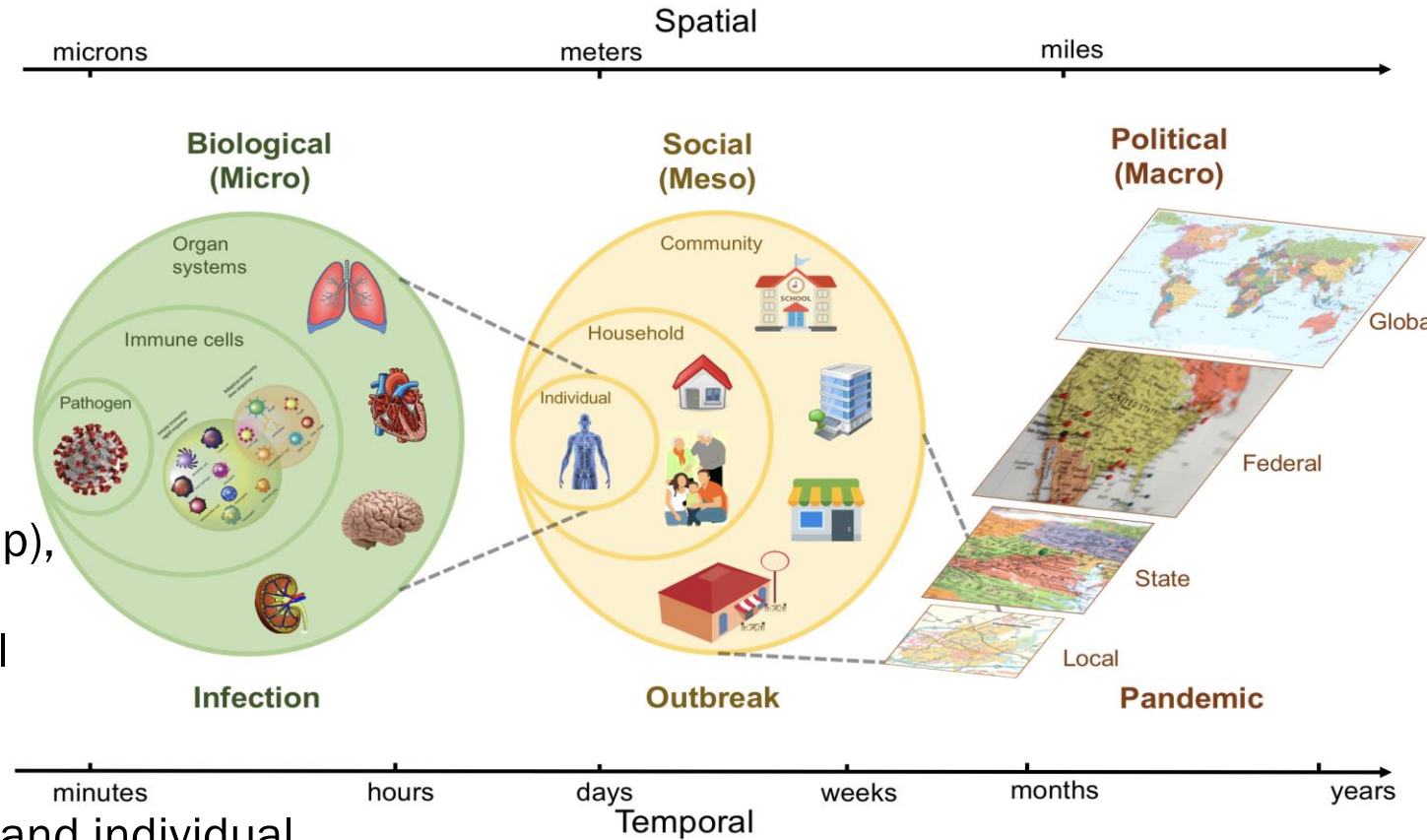
- Size of Data Sets
 - Observational and simulated data for global problems
- Noisy and sparse, Time lagged, Non Stationary and often not in computable form nor linked
 - Reasoning across these data sets becomes challenging
- Privacy, anonymity, security and commercial concerns
 - Individualized privacy preserving data is hard to get



Need: Federated and generalizable machine Learning models trained with limited and noisy data.

Scale Challenge: Spatial, temporal and social scales

- Processes unfolding across temporal scales
 - Within host disease progression
 - Between host transmission
 - Individual behavioral change
 - Community outbreak response
 - Public health control measures
 - Global response coordination
 - Seasonality and waning immunity
- Spatial and Social Interaction Scale
 - House (building), neighborhood (block group), city; state, country and region
 - Household, neighborhood and country level contact network
- Individual and collective behavior
 - Organizations (months), Community (days) and individual (days)



Need: Multi-scale, multi-theory, multi-level network representations, analytical tools and simulations

Trust and Adequacy challenge

- Retrospective and predictive validity are not as useful in crisis situations when data is limited.
- External Validation
 - validate past predictions
 - update future projections
- Internal Validation
 - ensure structurally correct
- How do we gather and incorporate relevant data in real-time to:
 - when modeling assumptions cause models to fail to capture real-world dynamics?

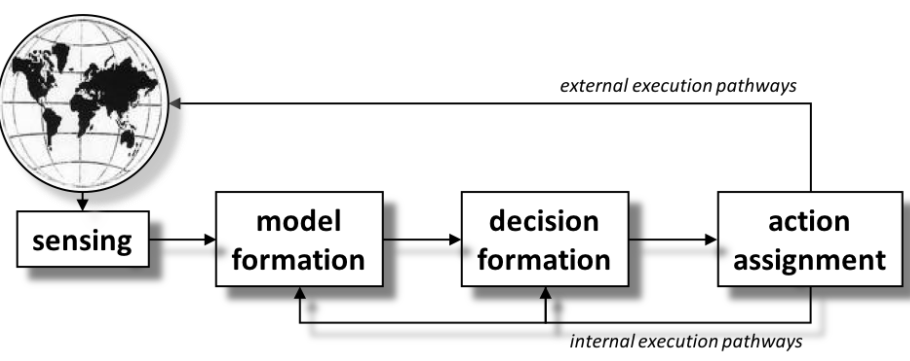


Additional challenges in: governance, ethics, logistics, diplomacy and one health are important but could not be covered due to time constraints

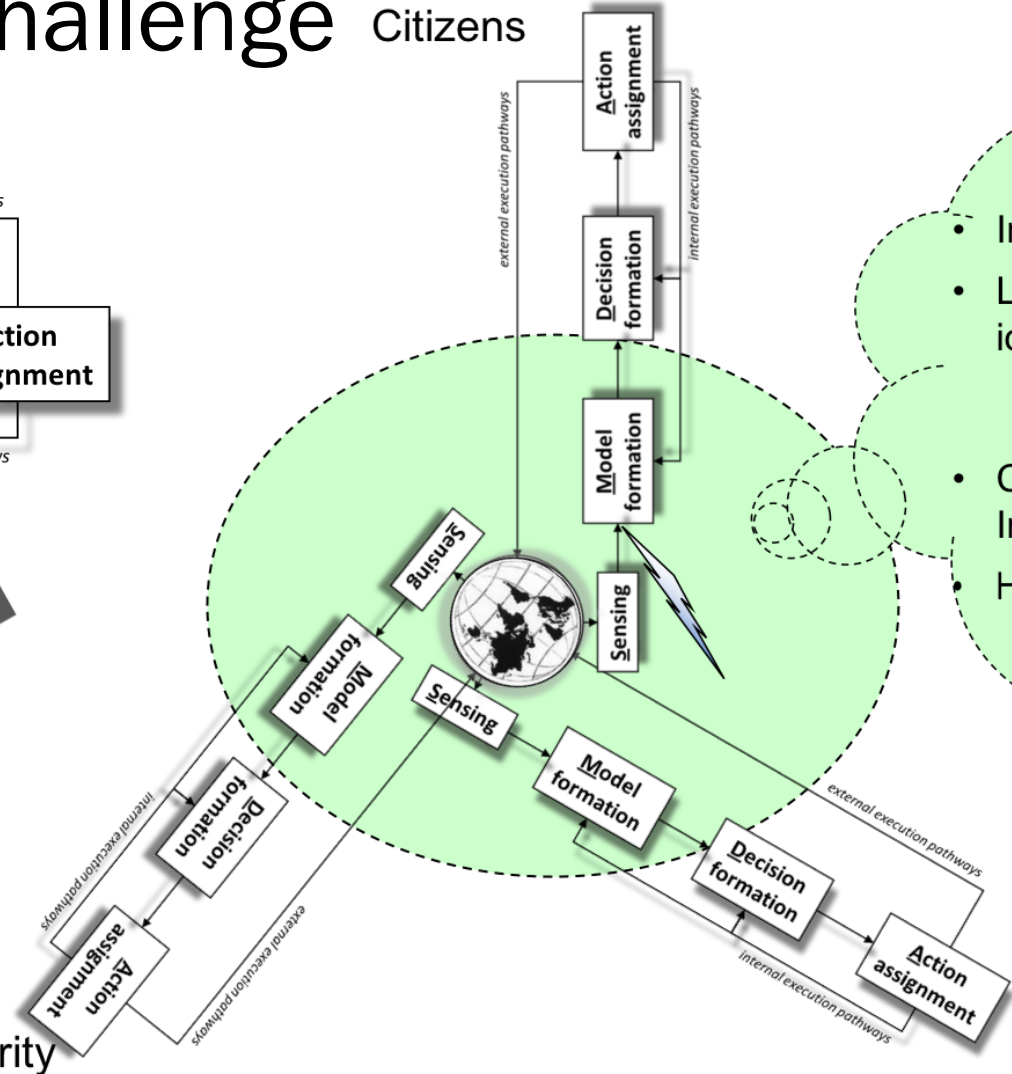
Need: New approaches for V&V, UQ and model adaptation for co-evolving networks

Decision making challenge

Citizens



Individual decision maker



US, State & Local Authority

On the ground responders: Doctors, Nurses, Educators, ...

- Information and actions are distributed
- Local models are compatible, but not identical or simple transformations
 - Differences may be important
 - Dynamics
- Context Specific Shared Synthetic Information
- Horizontal Integration
 - Non-attribution of sources
 - Privacy/ security

Need: Robust human-centered, decision making that is operational, works with diverse decision makers and is real-time

Pervasive, Personalized and Precision (P³) analytics for multiplexed networked systems

Pervasive: *Enable decision maker to make decisions at any, place, anytime and any device*

Personalized: *Enable decision maker to get personalized information that reflects her context*

Precise: *The decision maker should have precise information in space, time and context.*

Globally networked risks and how to respond

Dirk Helbing^{1,2}

Today's strongly connected, global networks have produced highly interdependent systems that we do not understand and cannot control well. These systems are vulnerable to failure at all scales, posing serious threats to society, even when external shocks are absent. As the complexity and interaction strengths in our networked world increase, man-made systems can become unstable, creating uncontrollable situations even when decision-makers are well-skilled, have all data and technology at their disposal, and do their best. To make these systems manageable, a fundamental redesign is needed. A 'Global Systems Science' might create the required knowledge and paradigm shift in thinking.

Globalization and technological revolutions are changing our planet. Today we have a worldwide exchange of people, goods, money, information, and ideas, which has produced many new opportunities, services and benefits for humanity. At the same time, however, the underlying networks have created pathways along which dangerous and damaging events can spread rapidly and globally. This has increased systemic risks¹ (see Box 1). The related societal costs are huge.

When analysing today's environmental, health and financial systems or our supply chains and information and communication systems, one finds that these systems have become vulnerable on a planetary scale. They are challenged by the disruptive influences of global warming, disease outbreaks, food (distribution) shortages, financial crashes, heavy solar storms, organized (cyber-)crime, or cyberwar. Our world is already facing some of the consequences: global problems such as fiscal and economic crises, global migration, and an explosive mix of incompatible interests and cultures, coming along with social unrests, international and civil wars, and global terrorism.

In this Perspective, I argue that systemic failures and extreme events are consequences of the highly interconnected systems and networked risks humans have created. When networks are interdependent^{2,3}, this makes them even more vulnerable to abrupt failures^{4,5}. Such interdependencies in our 'hyper-connected world'⁶ establish 'hyper-risks' (see Fig. 1). For example, today's quick spreading of emergent epidemics is largely a result of global air traffic, and may have serious impacts on our global health, social and economic systems⁷⁻⁹. I also argue that initially beneficial trends such as globalization, increasing network densities, sparse use of resources, higher complexity, and an acceleration of institutional decision processes may ultimately push our anthropogenic (man-made or human-influenced) systems¹⁰ towards systemic instability—a state in which things will inevitably get out of control sooner or later.

Many disasters in anthropogenic systems should not be seen as 'bad luck', but as the results of inappropriate interactions and institutional settings. Even worse, they are often the consequences of a wrong understanding due to the counter-intuitive nature of the underlying system behaviour. Hence, conventional thinking can cause fateful decisions and the repetition of previous mistakes. This calls for a paradigm shift in thinking: systemic instabilities can be understood by a change in perspective from a component-oriented to an interaction- and network-oriented view. This also implies a fundamental change in the design and management of complex dynamical systems.

The FuturICT community¹¹ (see <http://www.futurict.eu>), which involves thousands of scientists worldwide, is now engaged in establishing a

'Global Systems Science', in order to understand better our information society with its close co-evolution of information and communication technology (ICT) and society. This effort is allied with the 'Earth system science'¹⁰ that now provides the prevailing approach to studying the physics, chemistry and biology of our planet. Global Systems Science wants to make the theory of complex systems applicable to the solution of global-scale problems. It will take a massively data-driven approach that builds on a serious collaboration between the natural, engineering, and social sciences, aiming at a grand integration of knowledge. This approach to real-life techno-socio-economic-environmental systems⁸ is expected to enable new response strategies to a number of twenty-first century challenges.

BOX 1

Risk, systemic risk and hyper-risk

According to the standard ISO 31000 (2009; http://www.iso.org/iso/catalogue_detail?csnumber=43170), risk is defined as "effect of uncertainty on objectives". It is often quantified as the probability of occurrence of an (adverse) event, times its (negative) impact (damage), but it should be kept in mind that risks might also create positive impacts, such as opportunities for some stakeholders.

Compared to this, systemic risk is the risk of having not just statistically independent failures, but interdependent, so-called 'cascading' failures in a network of N interconnected system components. That is, systemic risks result from connections between risks ('networked risks'). In such cases, a localized initial failure ('perturbation') could have disastrous effects and cause, in principle, unbounded damage as N goes to infinity. For example, a large-scale power blackout can hit millions of people. In economics, a systemic risk could mean the possible collapse of a market or of the whole financial system. The potential damage here is largely determined by the size N of the networked system.

Even higher risks are implied by networks of networks^{12,13}, that is, by the coupling of different kinds of systems. In fact, new vulnerabilities result from the increasing interdependencies between our energy, food and water systems, global supply chains, communication and financial systems, ecosystems and climate¹⁰. The World Economic Forum has described this situation as a hyper-connected world¹, and we therefore refer to the associated risks as 'hyper-risks'.

¹ETH Zurich, Clausiusstrasse 50, 8092 Zurich, Switzerland. ²Risk Center, ETH Zurich, Swiss Federal Institute of Technology, Scheuchzerstrasse 7, 8092 Zurich, Switzerland.

**Some background
information**