

Chasing the Pandemic

Computational Models in the Fight against COVID-19

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Acknowledgments



- ❖ Biocomplexity Institute COVID-19 Response Team
- ❖ Members of the Network Systems Science & Advanced Computing Division
- ❖ Scientific colleagues in CDC-coordinated Hubs
- ❖ Collaborators from Indian Institute of Science and Indian Statistical Institute

Federal sponsors



Virginia stakeholders



Virginia Department of
Emergency Management



Data partners



Google



Metaculus

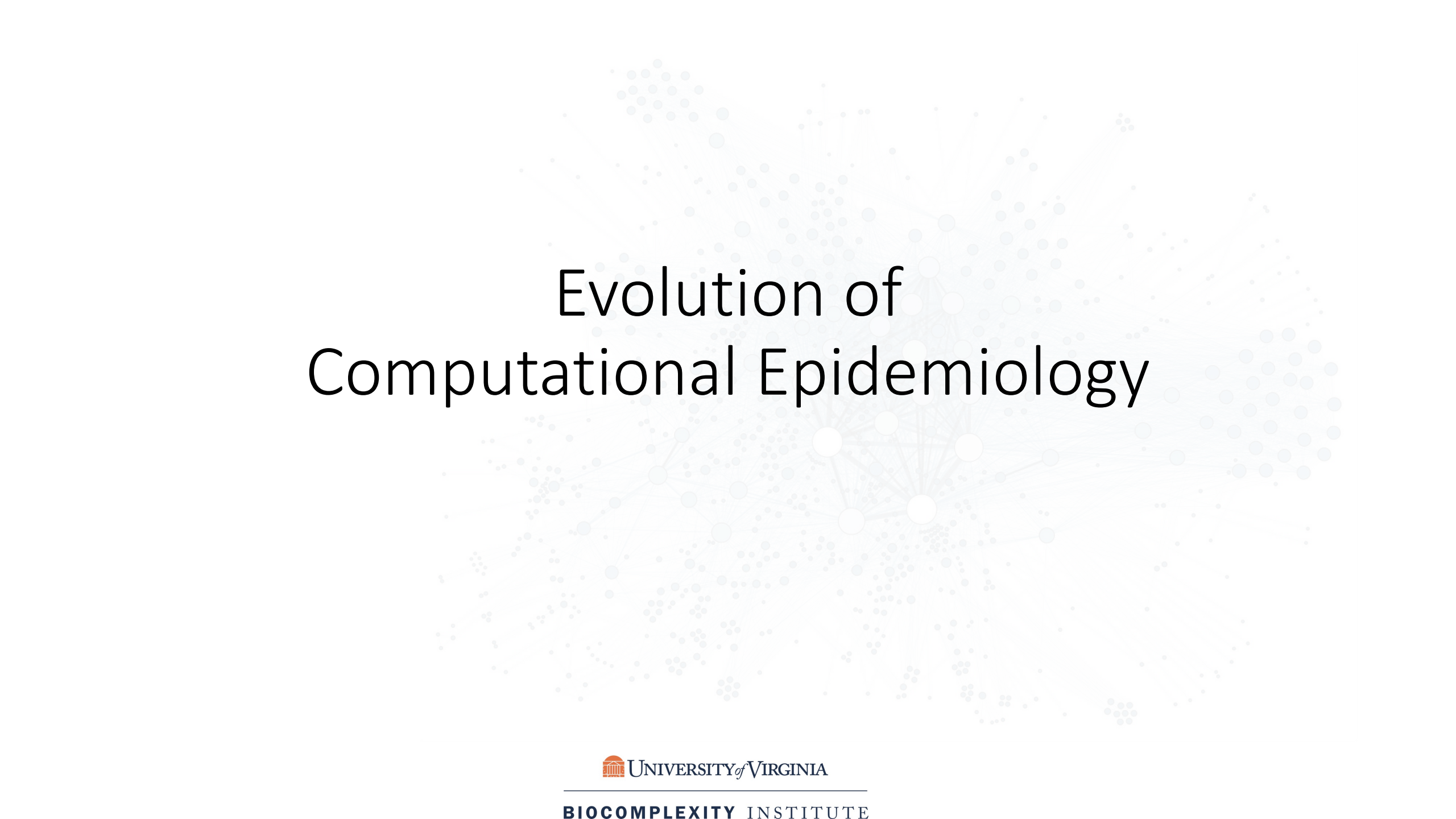


SAFEGRAPH



Overview

- Evolution of computational epidemiology
- COVID-19 pandemic response
- Act 1: Emergence and Early Spread
- Act 2: Tracking and Responding
- Act 3: Evolution and Integration
- Ongoing challenges

A complex network diagram with numerous nodes of varying sizes (small dots and larger circles) connected by thin lines, forming a dense web-like structure that fills the background of the slide.

Evolution of Computational Epidemiology

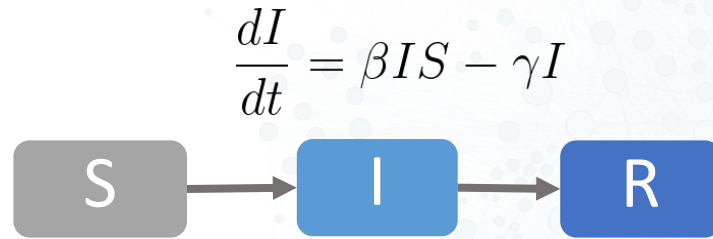
Mathematical models

SIR type models

Susceptible (S): never had the disease and is susceptible to being infected

Infected (I): currently has the disease and can infect other individuals

Recovered (R): does not have the disease, cannot infect others, and cannot be infected



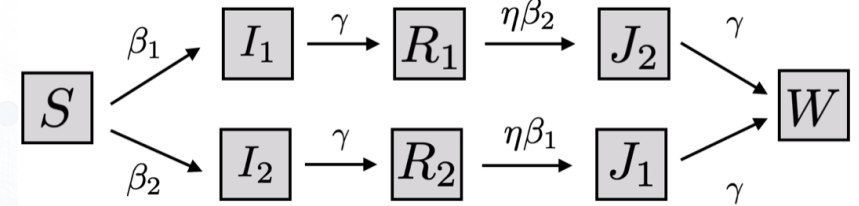
$$\frac{dI}{dt} = \beta IS - \gamma I$$

$$\frac{dS}{dt} = -\beta IS$$

$$\frac{dR}{dt} = \gamma I$$

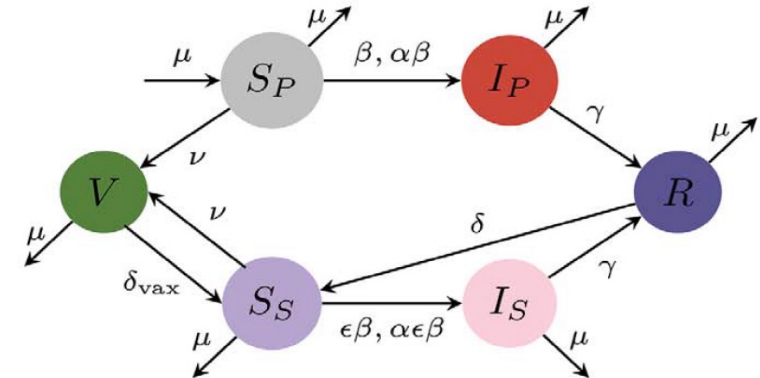
β - transmission/mixing rate
 $1/\gamma$ - mean infectious period

Extensions



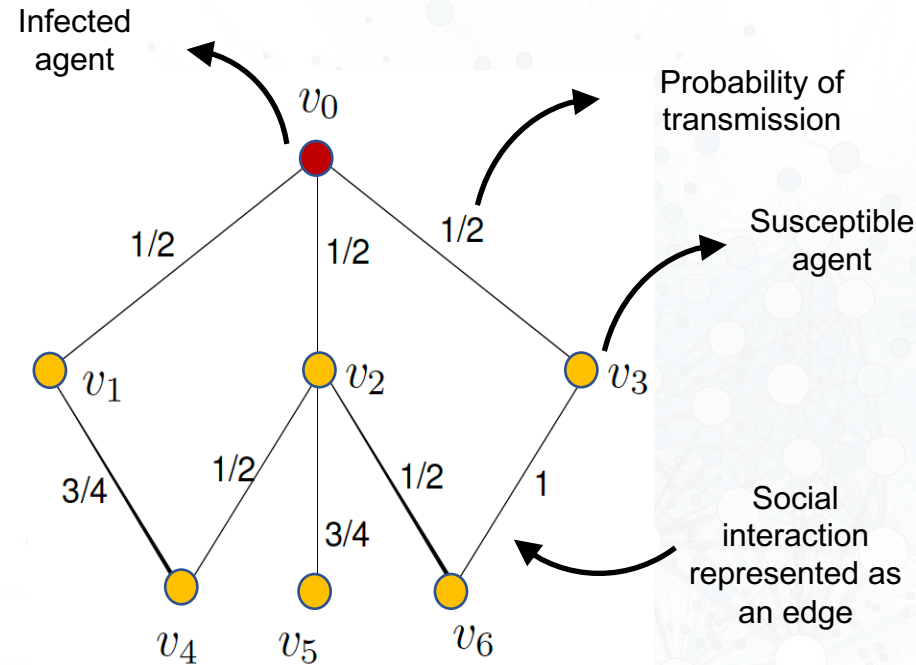
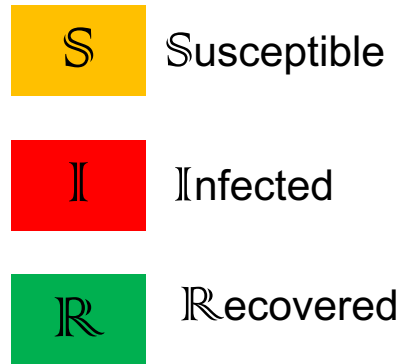
Two strain model

Source: Chadi Roy et al., Science 2020

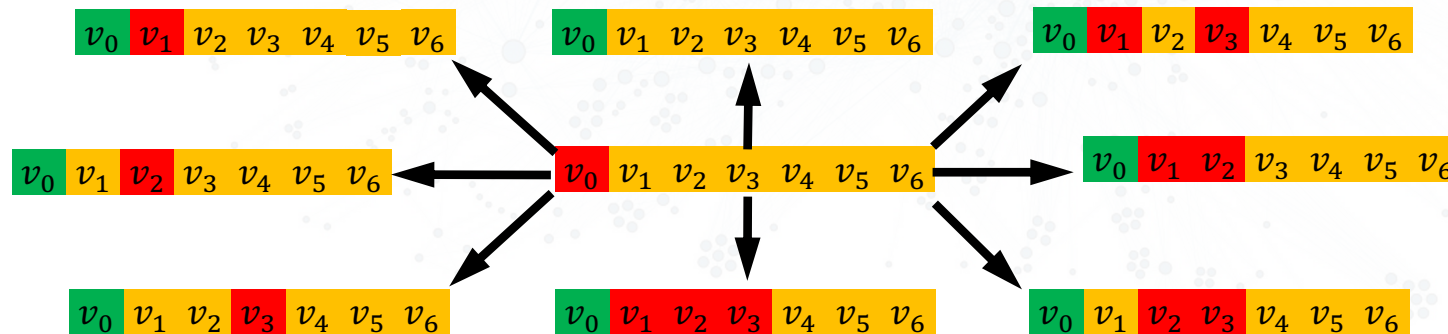


Natural immunity
 re-infections, and vaccines

Graphical dynamical systems



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



Current paradigms

Mechanistic models

Statistical/ML models

- Time-series methods
 - Autoregressive
 - Kalman Filter
 - Deep-learning (e.g., RNN)
- Ensemble methods
 - Bayesian moving average
- Useful for short-term forecasting

Metapopulation models

- Fully mixing subpopulations connected through a network
- Intermediate for network and ODE based models
- Useful for spatiotemporal or age-stratified modeling

Agent-based models

- Individual level representation through a dynamic contact network
- Could have additional representations for households, activity locations
- Can represent complex interventions

Statistical and Mechanistic models

Statistical models

Establishing a statistical (correlation) relationship between inputs and outputs

Requires large datasets, often homogeneous linked records

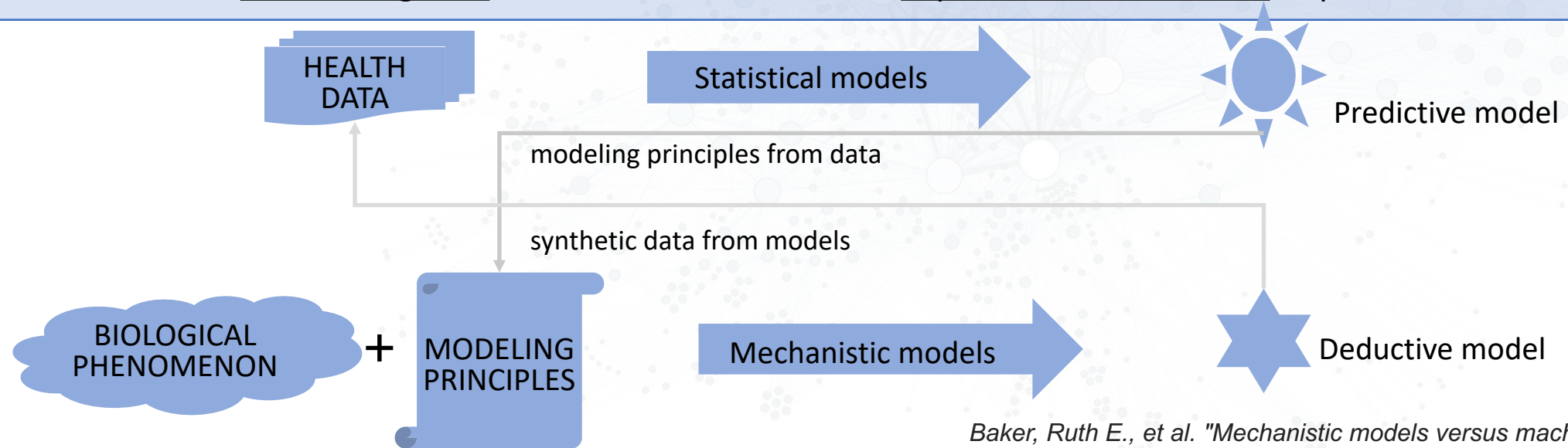
Can only make predictions that relate to patterns in the training data

Mechanistic models

Establishing a mechanistic (causal) relationship between inputs and outputs

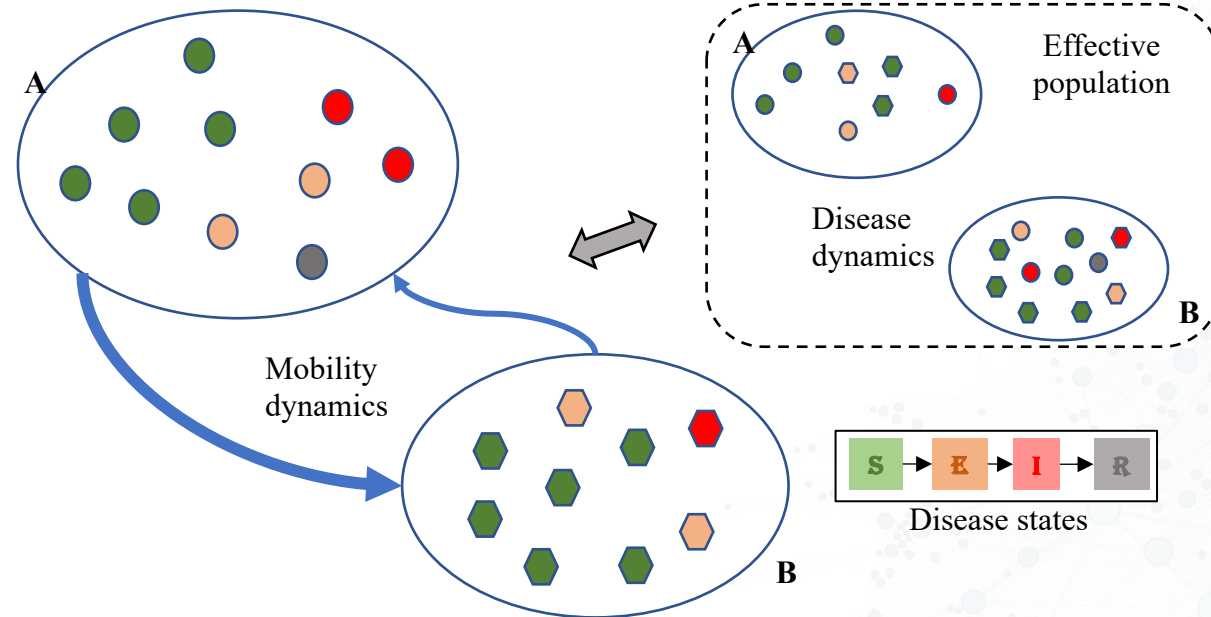
Can work with small datasets coming from diverse sources

Once validated, can be used for prediction where experiments are difficult to perform

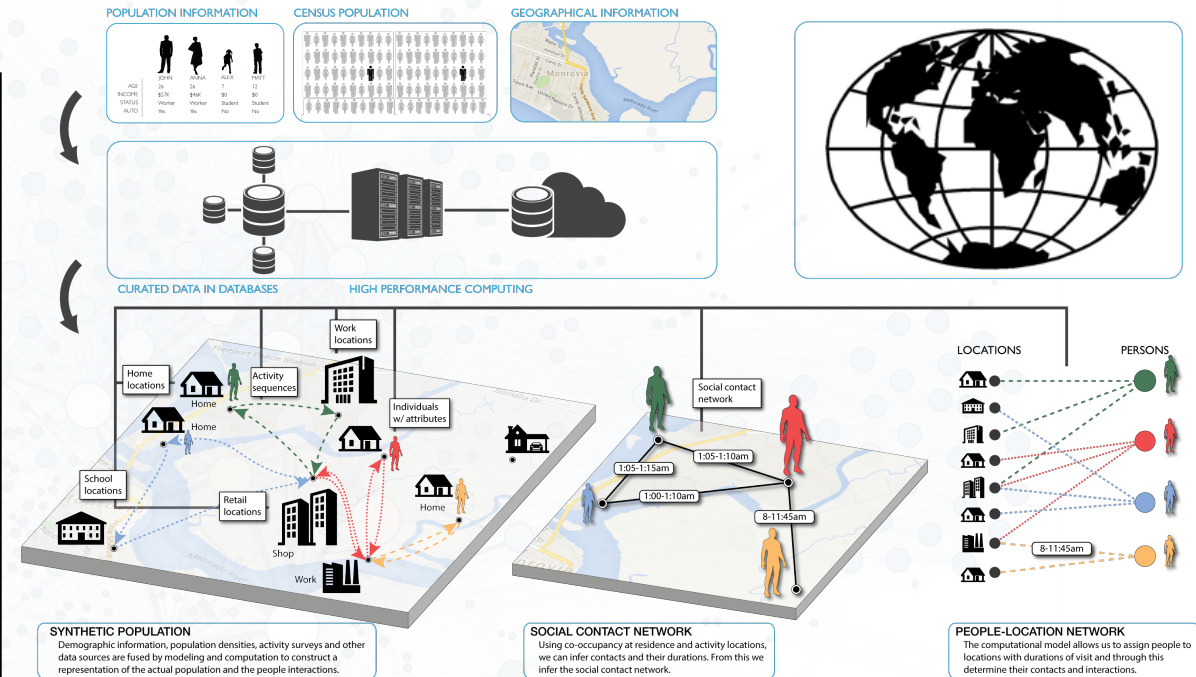


Baker, Ruth E., et al. "Mechanistic models versus machine learning, a fight worth fighting for the biological community?." Biology letters 14.5 (2018): 20170660.

Metapopulation and Agent-based models

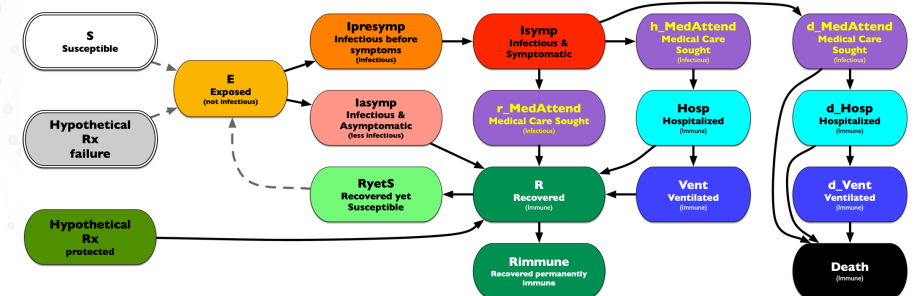


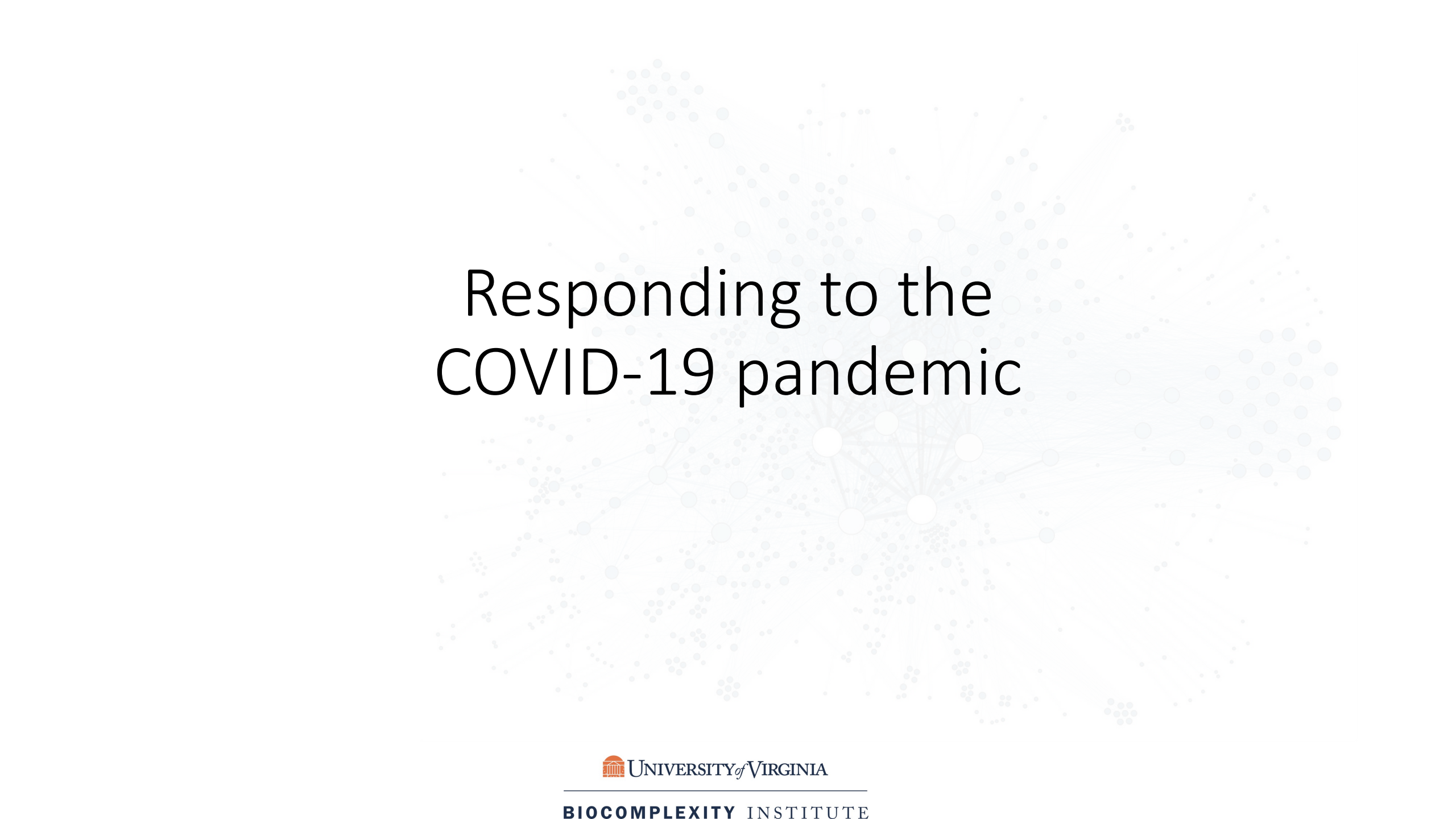
Digital twin representation



Each of the individual elements could be complex:

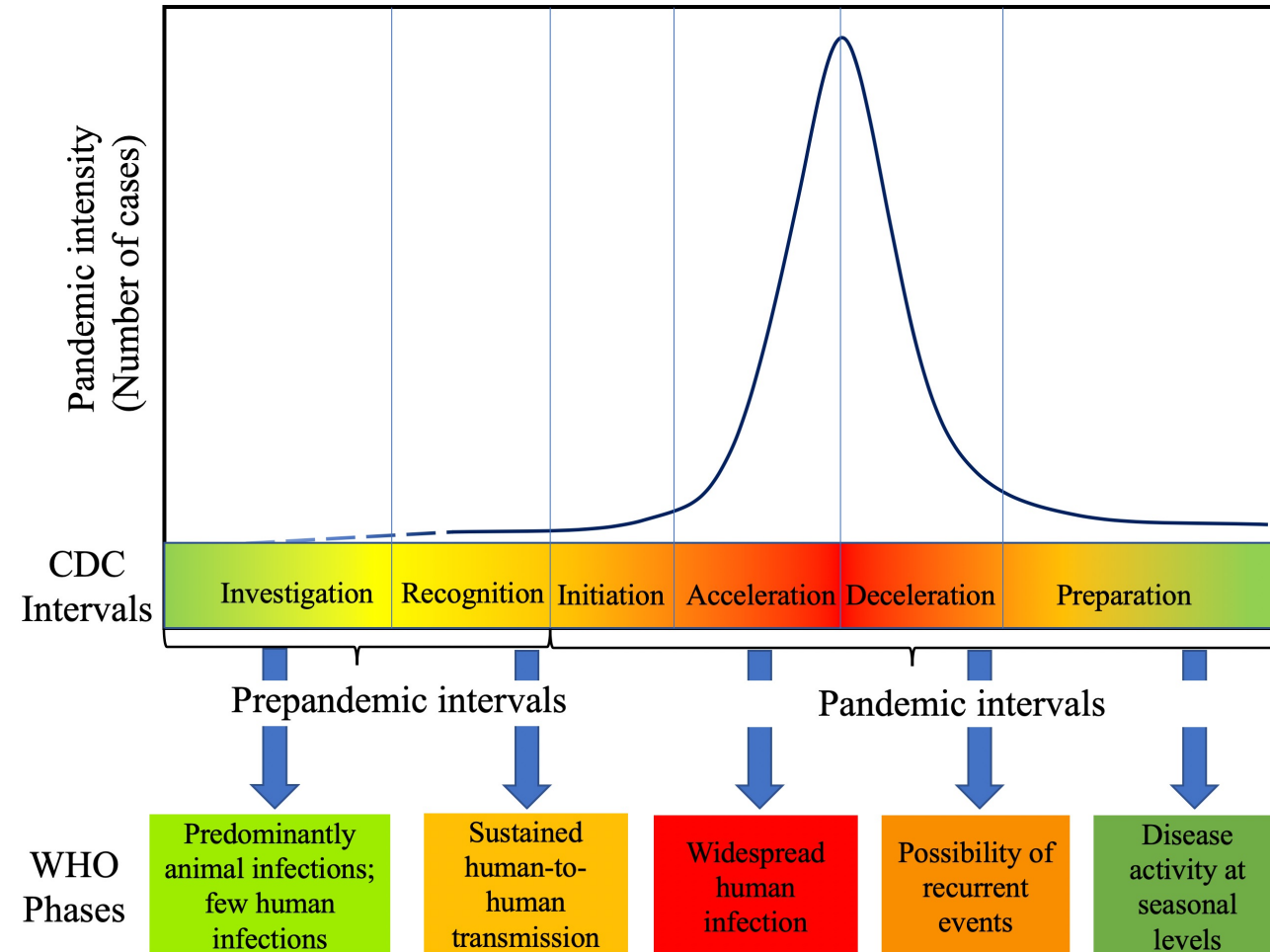
Disease progression
Contact/mixing representation
Types of interventions



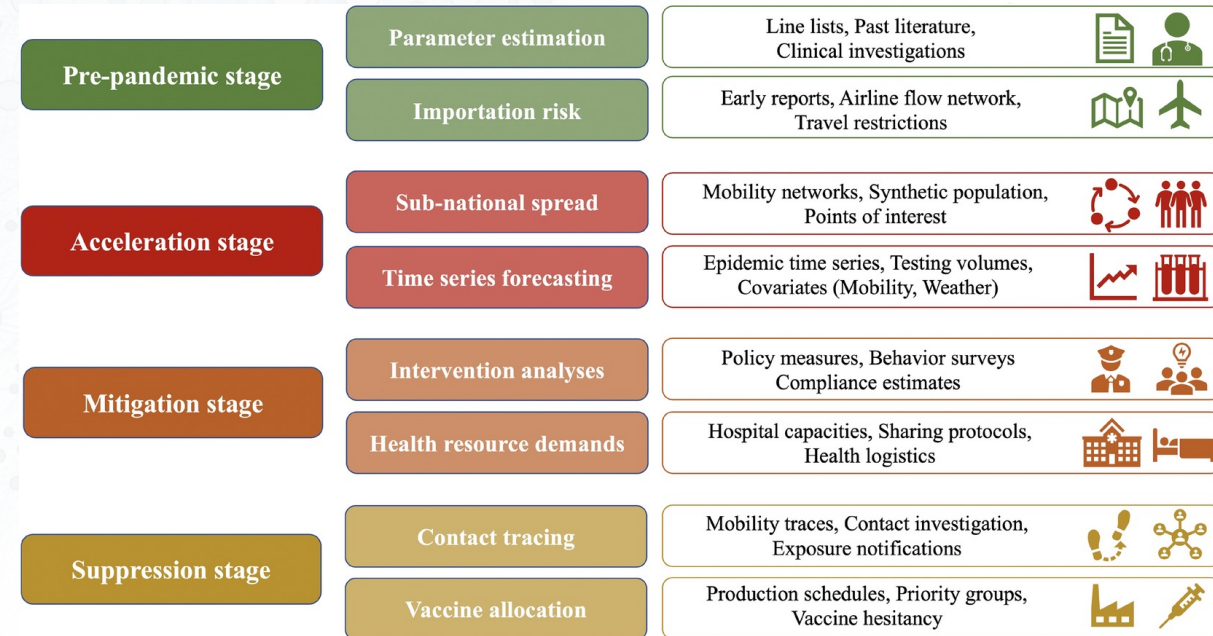
A complex network diagram with numerous nodes of varying sizes (small dots and larger circles) connected by thin lines, forming a dense web. The nodes are light blue and white, and the lines are light gray. The overall shape is roughly circular, with many connections radiating from a central area.

Responding to the COVID-19 pandemic

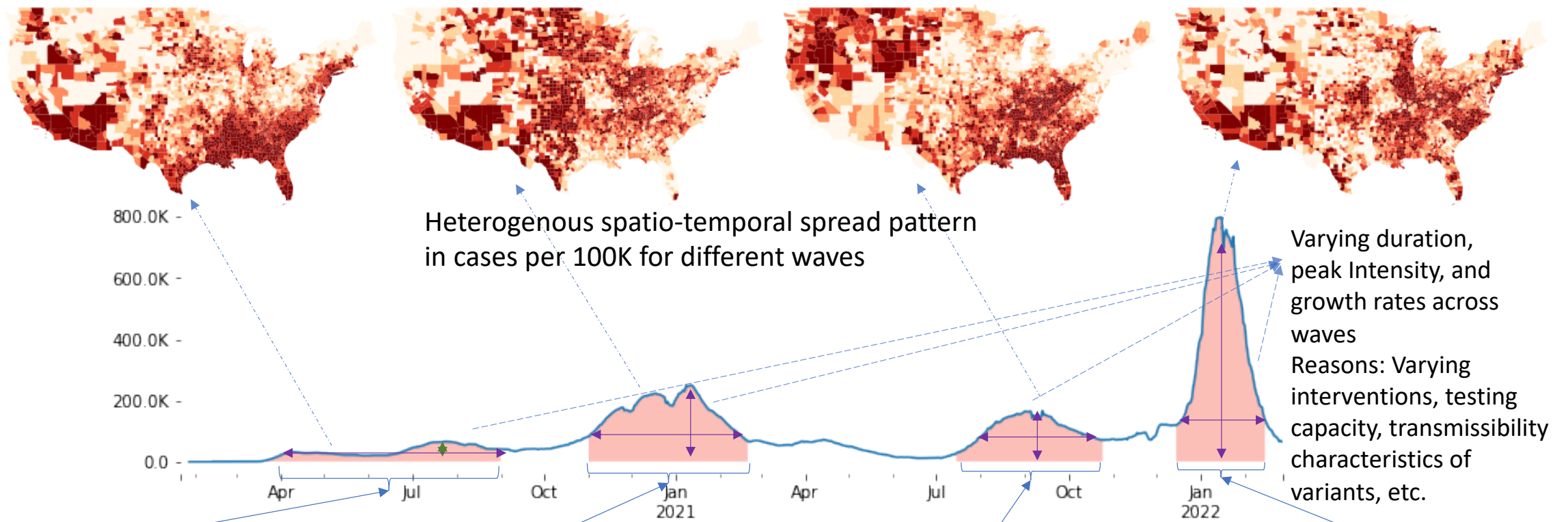
Modeling for different pandemic phases



- Different questions of interest across phases
- Data availability also changes over time
- Different modeling paradigms become relevant



Adiga, Aniruddha, et al. "Data-driven modeling for different stages of pandemic response." *Journal of the Indian Institute of Science* 100.4 (2020): 901-915.



First wave (wild type):

- Lack of immunity
- Mixing in the population during the initial phase

Measures:

- **Extreme restrictions** (lockdown)
- Mask wearing

Second wave:

- **Relaxed social interventions, holidays, university reopening**

Measures:

- **Behavioral adaptations**
- Mask wearing
- Partially vaccinated population

Third wave (Delta):

- Relaxed social interventions
- **Unvaccinated individuals**

Measures:

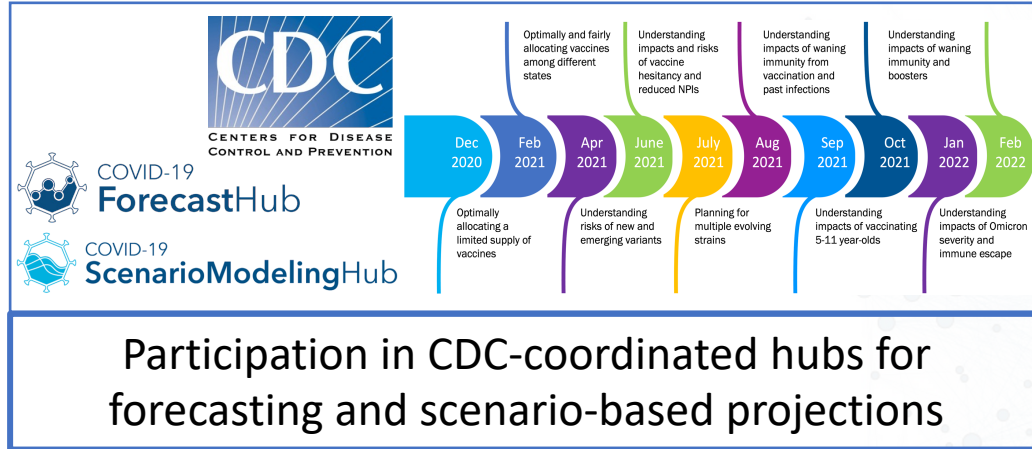
- **Vaccinations**
- Behavioral adaptations
- Mask wearing

Fourth wave (Omicron):

- **Immune escape**
 - Relaxed social interventions
- Measures:
- **Booster vaccinations**
 - Behavioral adaptations

First two years of the COVID-19 pandemic in the U.S.

Supporting COVID-19 Response in the US



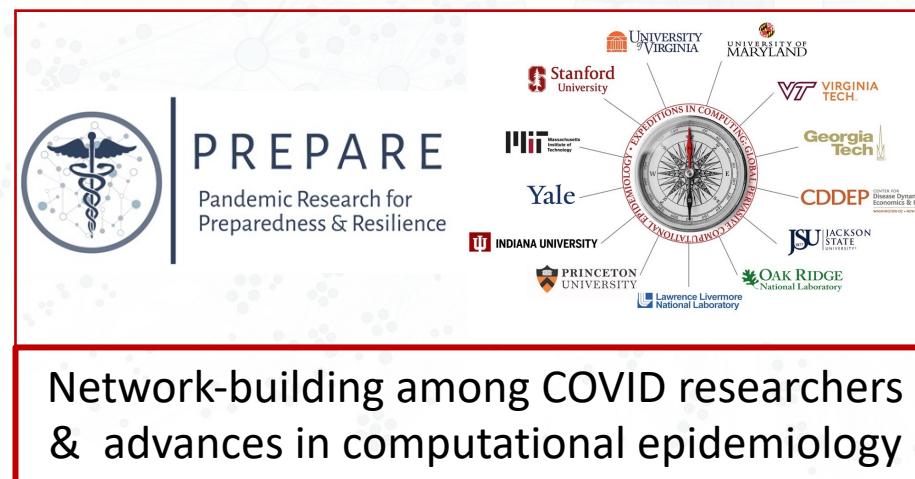
<https://nssac.github.io/covid-19/>

75+ publications

80+ scientists, staff & students

120+ weekly model updates

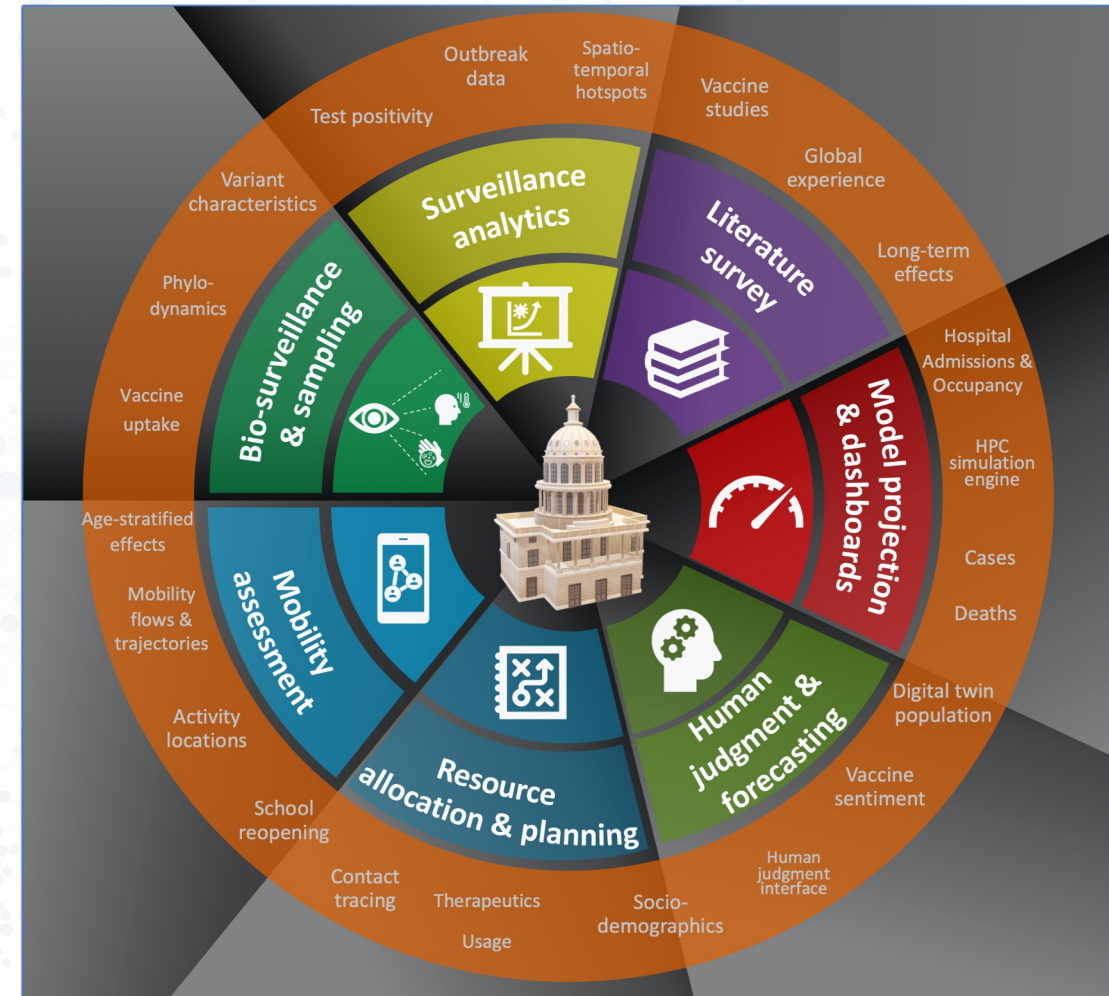
400+ quotes in the press



<https://prepare-vo.org/>
<https://computational-epidemiology.org/>

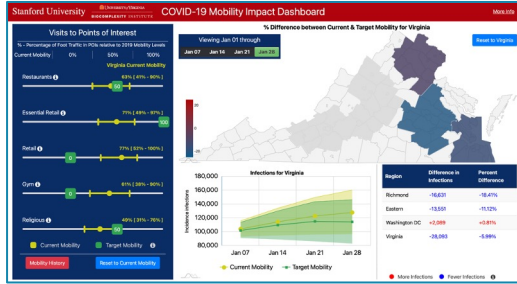
Engagement with the state of Virginia

- Multi-pronged approach to support VDH's COVID-19 response
- 120+ weekly briefings to policymakers and health practitioners
- Leveraging real-time datasets and HPC software workflows
- Multiple dashboards for policymakers



<https://www.vdh.virginia.gov/coronavirus/see-the-numbers/covid-19-modeling/>

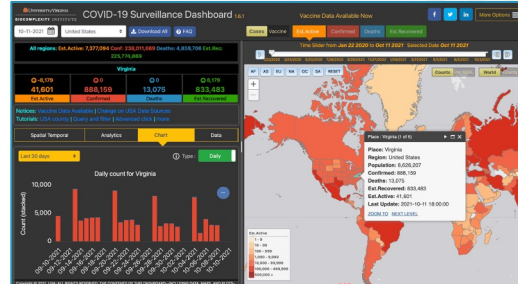
Contributions to public/policy communication



[Best Applied Paper Award for ACM SIGKDD 2021](#)

Mobility-based policy analysis tool

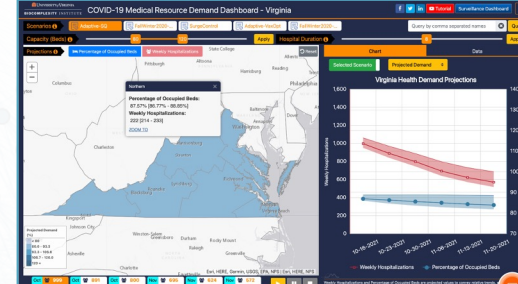
Interactive tool to analyze the impact on future cases based on altering mobility to different types of locations



<https://nssac.bii.virginia.edu/covid-19/dashboard/>

Global COVID-19 cases

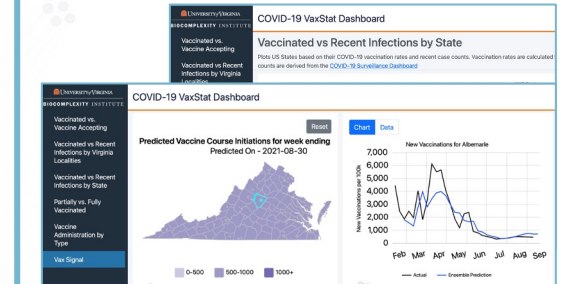
Provides interactive resource for monitoring and analyzing COVID-19 health statistics from around the world



<https://nssac.bii.virginia.edu/covid-19/vmrddash/>

Medical Resource Dashboard

Provides interactive resource for monitoring current and future projected hospitalization burden



<https://nssac.bii.virginia.edu/covid-19/vaxstatdashboard/>

Vaccination Statistics Dashboard

Provides predictive modeling and multiple reports assessing vaccination coverage

Advances in pandemic science & technology

Novel multi-model
ensemble framework
for short-term
forecasting

Phase classification
using auxiliary indicators

**Best Paper award in
IEEE BigData'22**

**Publications in
ACM KDD'21, IAAI'22**

Multi-strain tiered
immunity model for
scenario-based projections

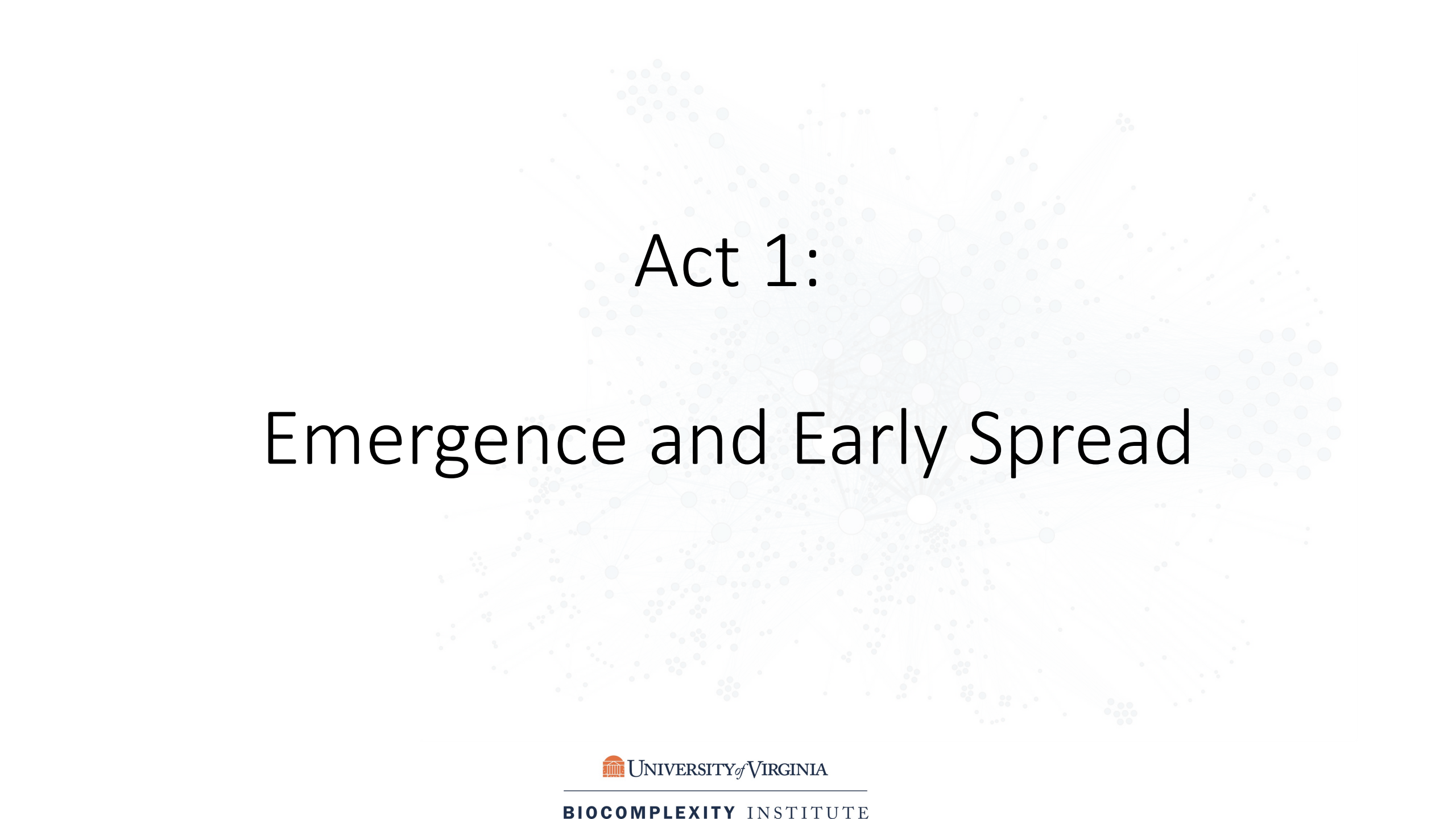
Open global datasets for
metapopulation
dynamics

**120+ weekly updates;
UVA Award on
Collaborative Excellence
in Public Service**

National scale agent-
based model with
hybrid HPC pipeline

Diverse case studies on
vaccine hesitancy &
uptake, economic
impact analyses

**Finalist in ACM Gordon
Bell Special Prize for
HPC COVID-19 Research
(2021)**

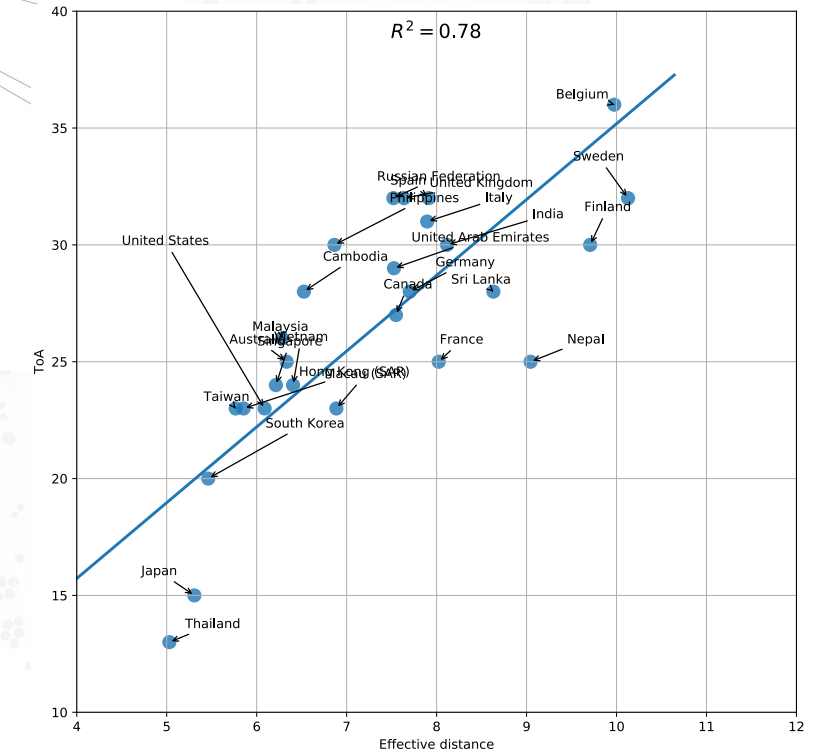
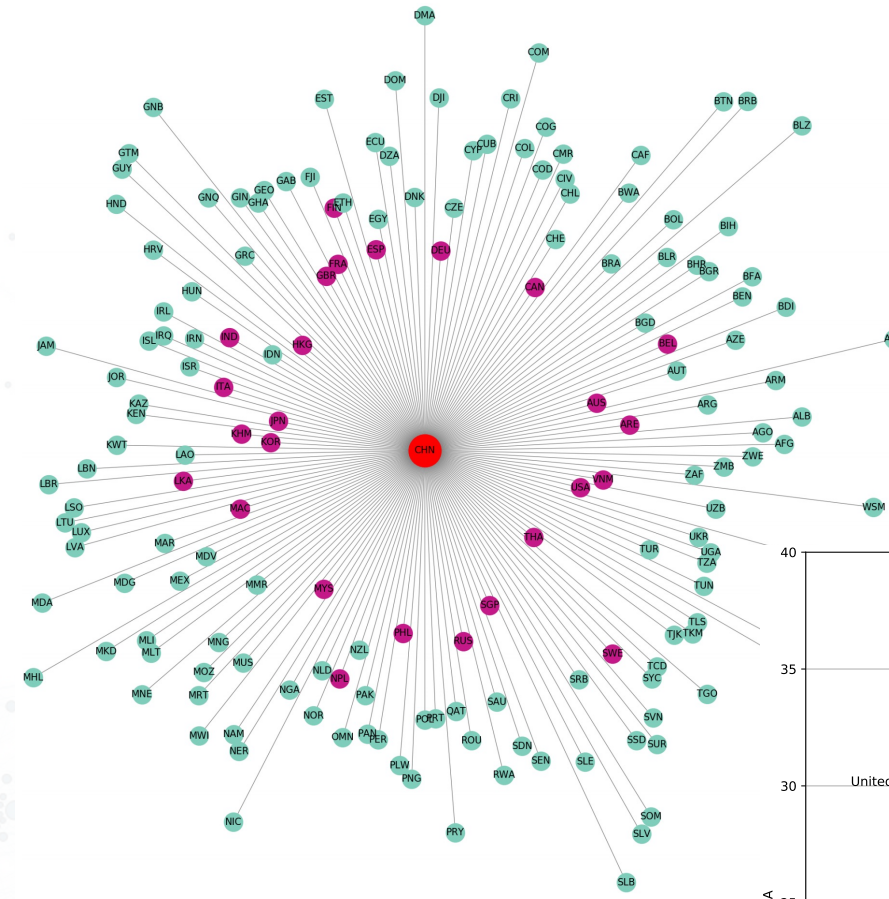
A complex network diagram with numerous nodes of varying sizes (small dots and larger circles) connected by thin lines, forming a dense web-like structure. The nodes are primarily light blue and white, with some larger white nodes acting as hubs. The background is a light gray gradient.

Act 1:

Emergence and Early Spread

Importation Risk (Feb 2020)

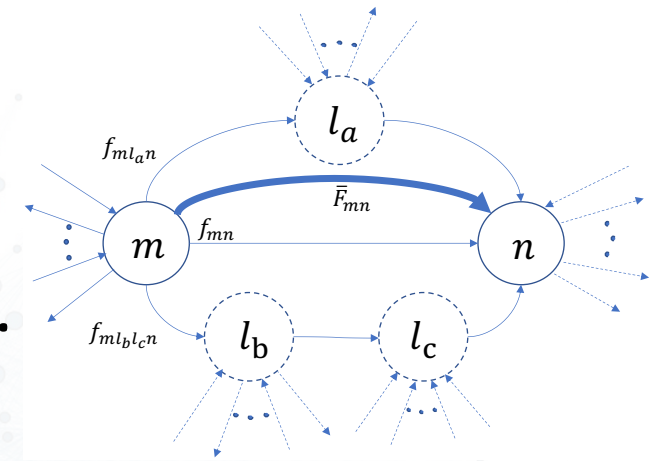
- Using International Airline data build international travel network from February 2019
- For COVID-19, treat China as the source of importation.
 - Data until Feb 12th justify this assumption
- Calculate effective distance between countries
 - based on volumes of air traffic and underlying dynamics
- Fit a linear model for COVID-19 official first reports
 - Arrival time of disease shown to match effective distance with a linear fit for H1N1 and SARS [Brockman et al. 2013]



Adiga, Aniruddha, et al. "Evaluating the impact of international airline suspensions on the early global spread of COVID-19." *MedRxiv* (2020).

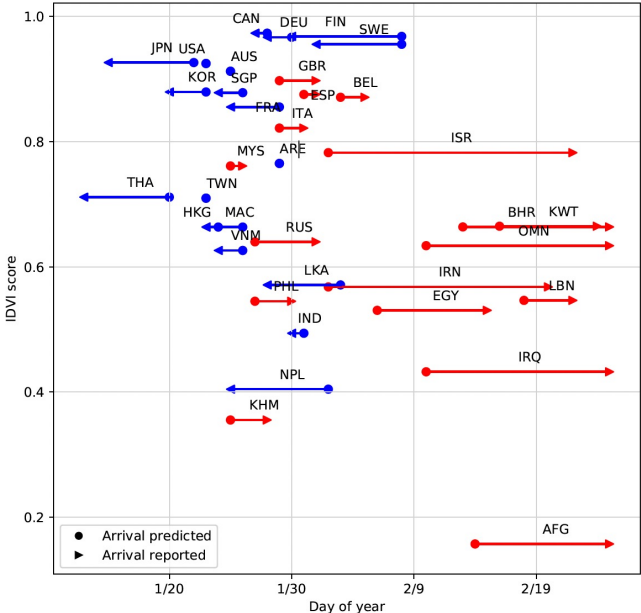
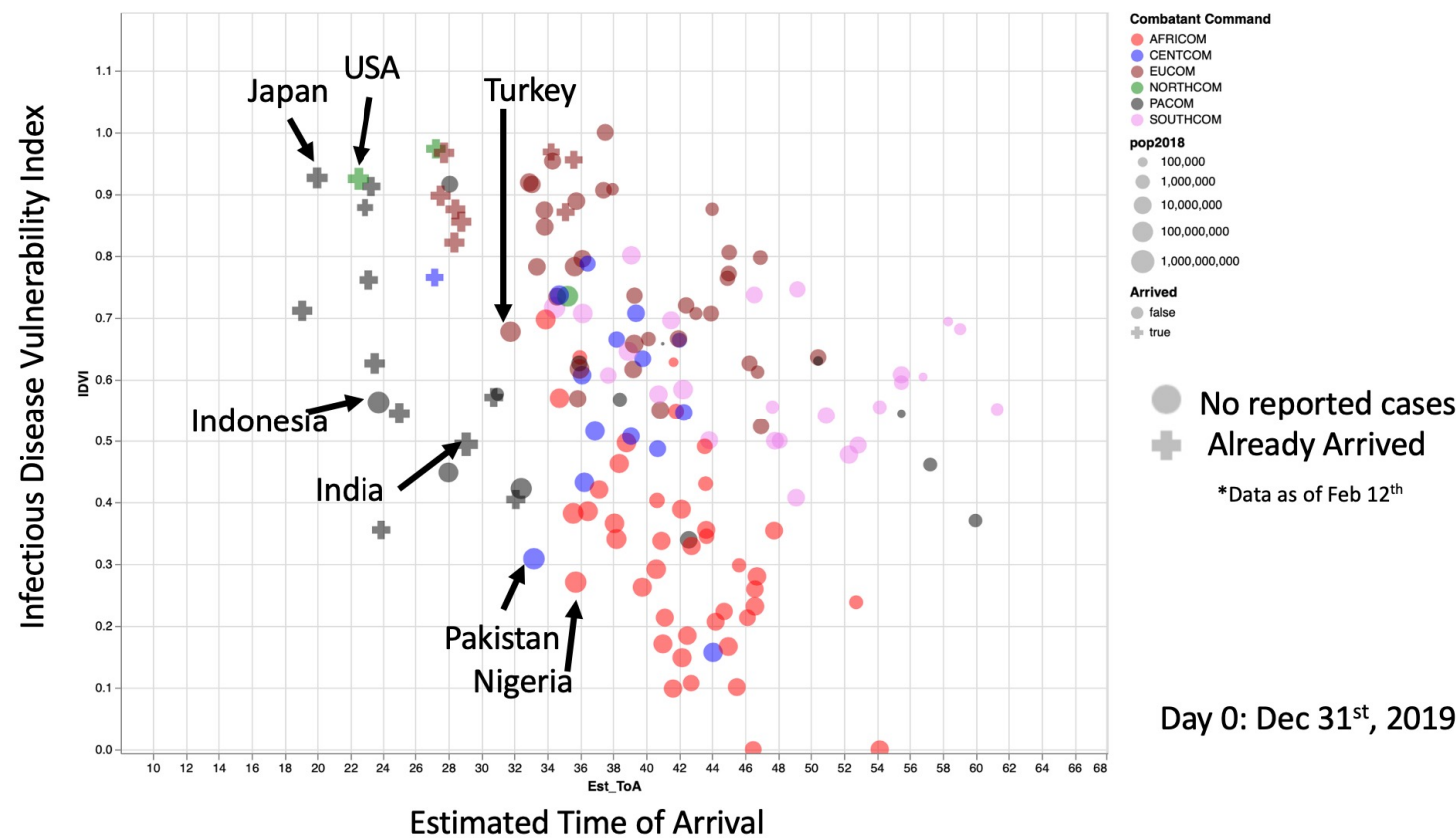
Effective distance computation

- Obtain source-origin flow using IATA data.
- We denote the flow between origin m and n as F_{mn} .
- Computation of F_{mn} :
 - Query all source-destination passenger volumes.
 - Volumes can correspond to direct or stop-over flights. For source WUH and destination SFO, possible routes WUH->SFO, WUH->FRA->SFO, WUH->HKG-> CDG->SFO.
 - Sum flows from all the individual routes to get F_{mn} .
- Computation of outflow probability $\bar{F}_{mn} = F_{mn} / \sum_k F_{mk}$.
- Effective distance $d_{mn}^{IATA} = 1 - \log \bar{F}_{mn}$.



Formulation adapted from:
Brockmann, Helbing, Science 2013

Relationship with geopolitical variables



Early or late reports than predicted

Score	Slope	R^2	p-value	std-error
Overall IDVI	-14.70	0.16	0.02	5.78
Demographic	-14.26	0.11	0.05	7.11
Healthcare	-12.82	0.06	0.15	8.63
Public health	-12.28	0.08	0.10	7.32
Disease dynamics	6.65	0.02	0.40	7.96
Political (domestic)	-13.35	0.24	0.002	4.09
Political (international)	-14.24	0.18	0.01	5.24
Economic	-7.23	0.05	0.19	5.43

Table 1. Relationship between IDVI scores and projected reporting delays. Overall IDVI explains about 16% of the variance in estimated reporting delays, while political domain scores (domestic and international) explain about 24% and 18% respectively ($p < 0.05$).

Provided estimated time before introduction to low IDVI countries

Quantifying the benefit of airline cancellations

Bloomberg had compiled list of all airline cancellations:

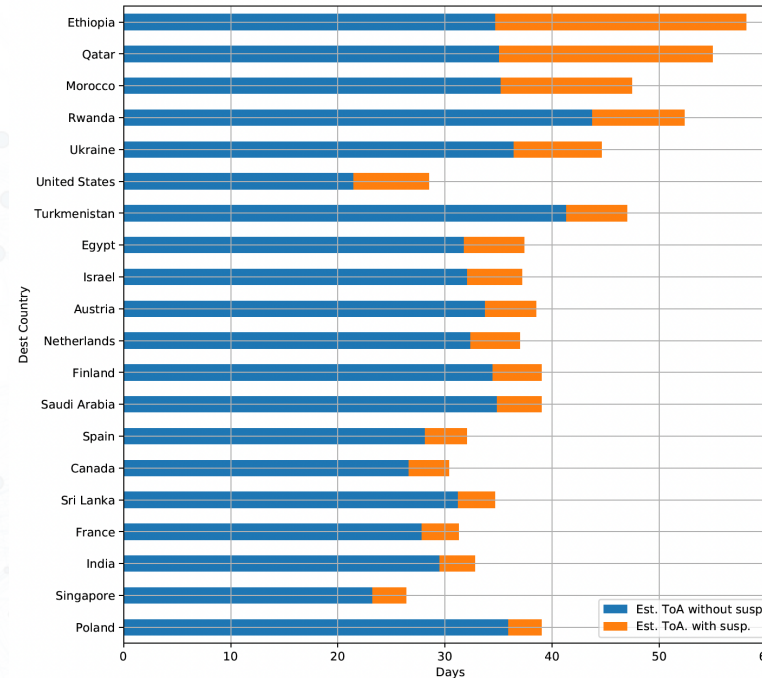
<https://www.bloomberg.com/graphics/2020-china-coronavirus-airlines-business-effects/>

Adjusting the historical flight network data using cancellation information to estimate “current” flight network

The Airlines Halting China Flights as Virus Outbreak Spreads

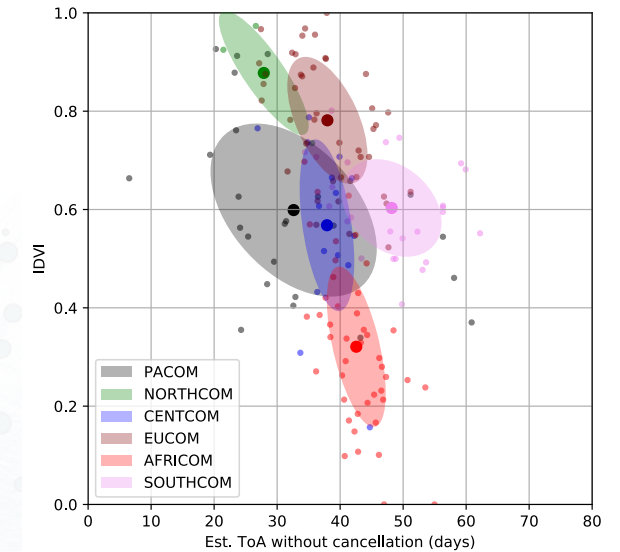
By [Demetrios Pogkas](#), [Cedric Sam](#) and [Chloe Whiteaker](#)
Updated: February 11, 2020, 1:15 AM EST

The coronavirus outbreak has disrupted flights to and from China, one of the world's busiest travel markets, as airlines around the globe halt service.

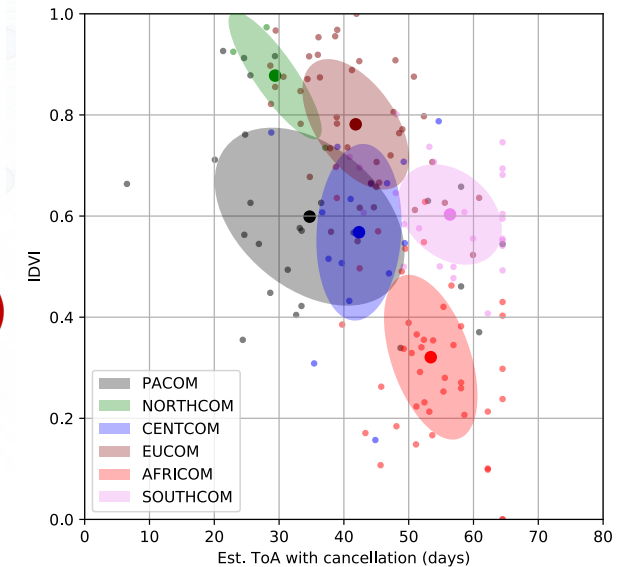


Showed quantifiable (although minimal) impact of airline cancellations

Without cancellations



With cancellations



Flattening the curve in Virginia (April 2020)



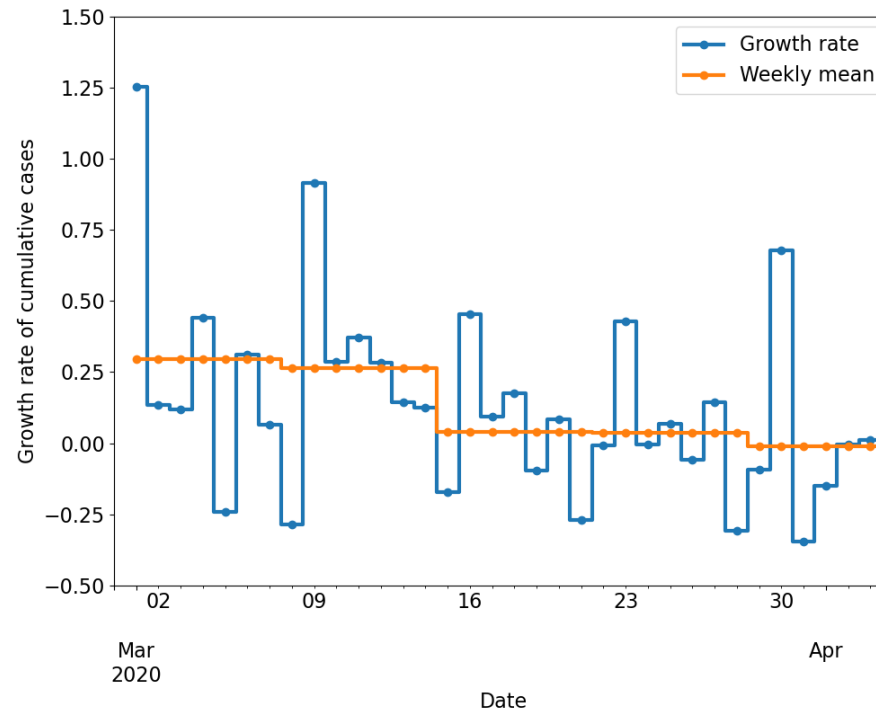
Commonwealth of Virginia
Office of the Governor

Executive Order

NUMBER FIFTY-ONE (2020)

DECLARATION OF A STATE OF EMERGENCY
DUE TO NOVEL CORONAVIRUS (COVID-19)

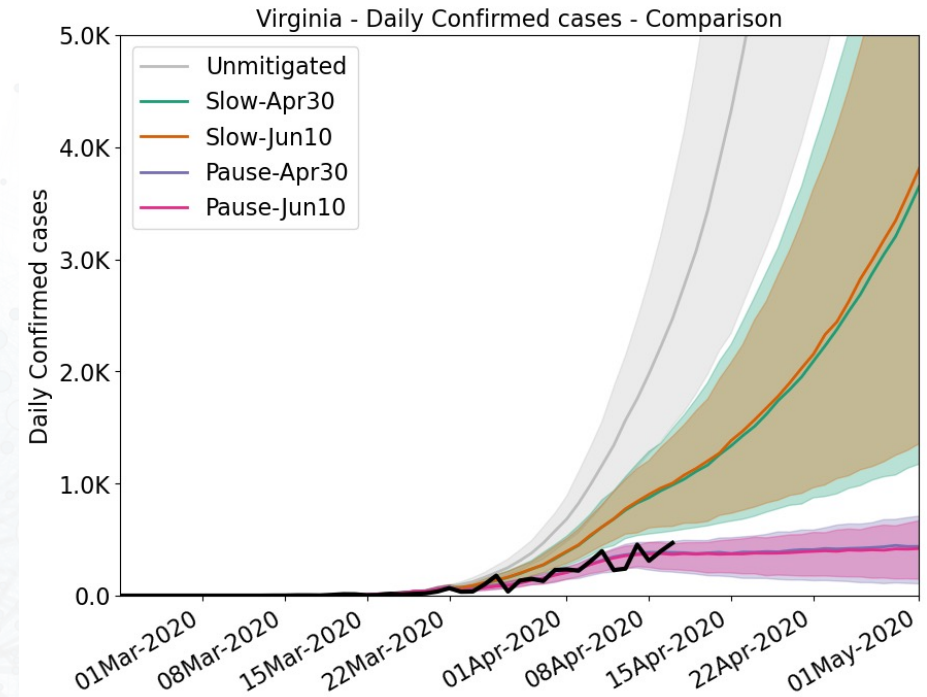
March 12th, 2020



Impact of stay-at-home orders (March 15th)

- Weekly growth rate changed from 0.3 $\rightarrow$ 0.03
- Change in Reproduction number: 2.2 $\rightarrow$ 1.1

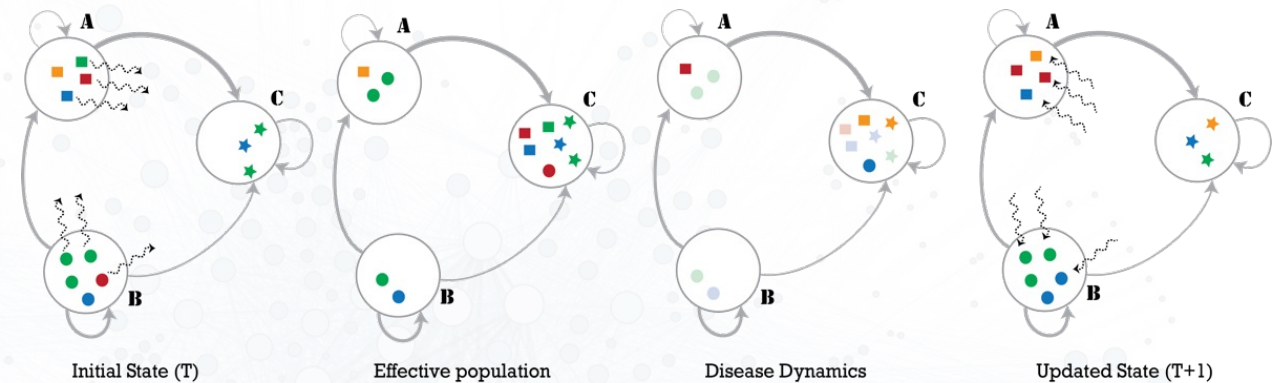
Confirmed cases



Duration (lift date)	Intensity	Short Name
Apr 30 th	Slowing	Slow - Apr30
June 10 th	Slowing	Slow - Jun10
Apr 30 th	Pausing	Pause - Apr30
June 10 th	Pausing	Pause - Jun10
None	Unmitigated	Unmitigated

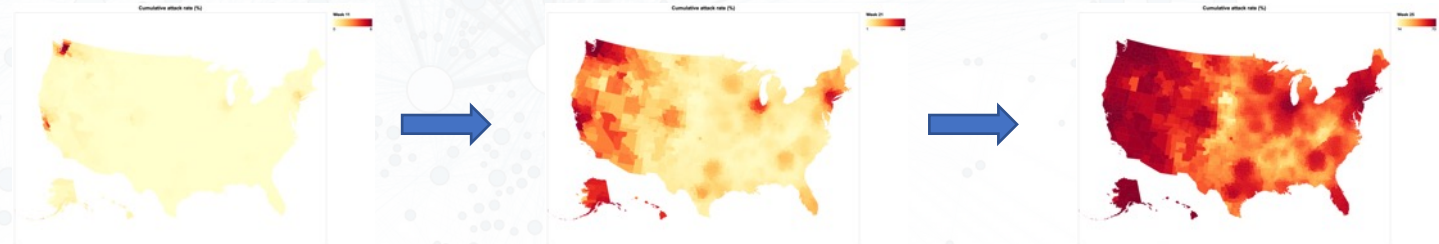
Simulation Engine – PatchSim

- Metapopulation model
 - Represents each county and its interactions as a single patch
 - Extended SEIR disease representation, including asymptomatic infections and treatments
 - Mitigations affect both disease dynamics and population interactions
- **Transmission:** parameters are calibrated to the observed case counts
 - **Reproductive number:** 2.1 - 2.3
 - **Infectious period** (time of infectiousness before full isolation): 3.3 to 5 days
- **Initial infections:** Start infections from confirmed cases by county
 - Timing and location based on onset of illness from VDH data
 - Assume 15% detection rate, so one confirmed case becomes ~7 initial infections



S → E → I → R

Susceptible → Exposed → Infectious → Removed



Venkatramanan, Srinivasan, et al. "Optimizing spatial allocation of seasonal influenza vaccine under temporal constraints." *PLoS Computational Biology* 15.9 (2019): e1007111.

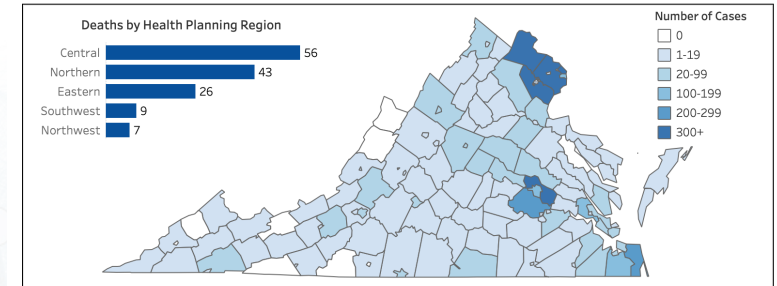
<https://github.com/nssac/patchsim>

Calibration Approach

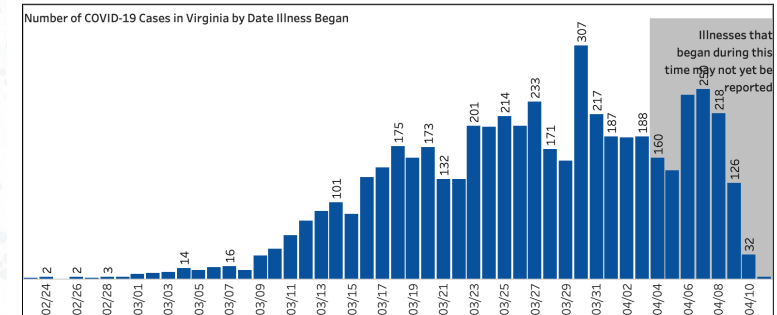
- **Data:**
 - County level case counts by date of onset (from VDH)
 - Confirmed cases for model fitting
- **Model:** PatchSim initialized with disease parameter ranges from literature
- **Calibration:** fit model to observed data
 - Search transmissibility and duration of infectiousness
 - Markov Chain Monte Carlo (MCMC) particle filtering finds best fits while capturing uncertainty in parameter estimates
- **Project:** future cases and outcomes using the trained particles
- Other parameters from: CDC COVID-19 Modeling Team. "Best Guess" scenario. Planning Parameters for COVID-19 Outbreak Scenarios. Version: 2020-03-31

COVID-19 Cases in Virginia

Number of People Tested^	Total Cases*	Total Hospitalizations**	Total Deaths
39,985	5,274	872	141

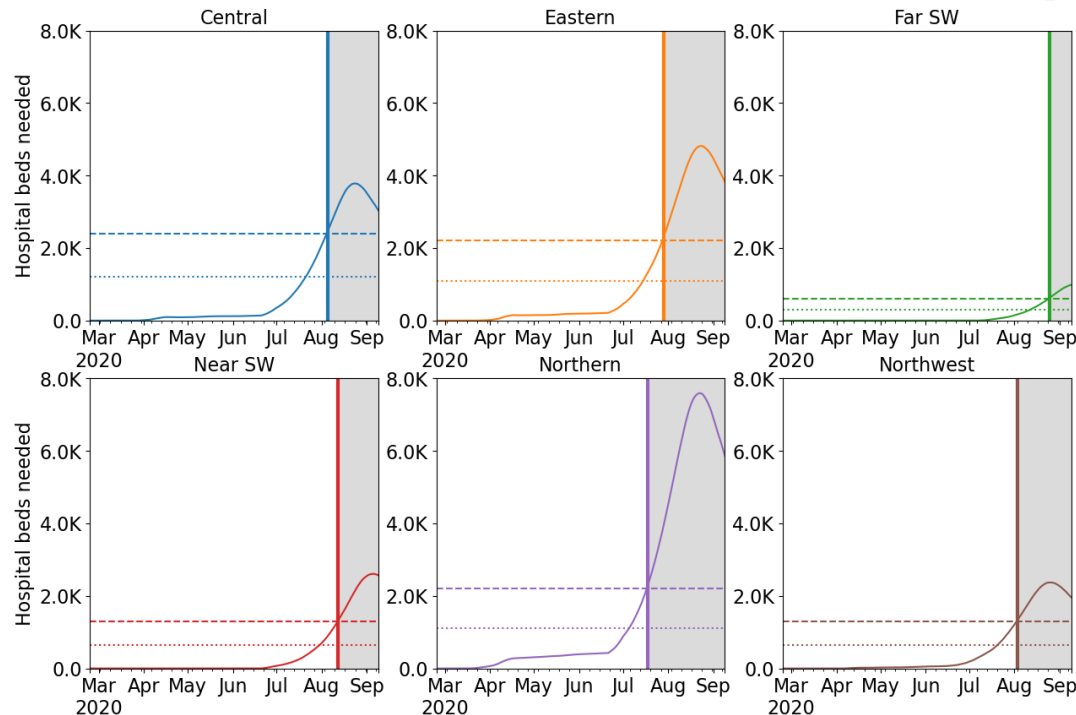


Health District	Locality	Number of Cases
Alexandria	Alexandria	198
Alleghany	Alleghany	4
	Botetourt	23
	Covington	1
	Craig	2
	Roanoke County	14
	Salem	1
Arlington	Arlington	366
Central Shenandoah	Augusta	17
	Buena Vista City	4
	Harrisonburg	81
	Lexington	3
	Rockbridge	3
	Rockingham	43



Operational impact on Field hospitals

Capacities by Region – Pause June 10



As of April 13, 2020, model estimated at least 3 months of lag before hitting hospital capacity under the "Pause" scenario

HEALTH & MEDICINE

U.Va.'s coronavirus model projects Virginia will have enough hospital capacity in next few months

By Peter Costou and Gary A. Harkl
The Virginian-Pilot • Apr 13, 2020 at 1:32 pm



Expand



Gov. Ralph Northam, left, speaks, accompanied by state Secretary of Health and Human Resources Dr. Daniel Carey, right, during a news conference on the state's preparedness for the coronavirus at the Capitol in Richmond, Va., on Wednesday, Mar. 4, 2020. (AP Photo/Steve Helber) (Steve Helber/AP)

Apr 13, 2020

Virginia is 'pivoting away' from field hospitals

Apr 17, 2020

Dr. Danny Avula of Richmond/Henrico health departments says hospitals likely can handle coming surge.

PUBLISHED APRIL 17, 2020 BY KATE ANDREWS

virginia

Virginia is "pivoting away" from needing field hospitals to handle patient overflow because health systems believe they'll be able to manage any surge in COVID-19 cases, said Dr. Danny Avula, the director of Richmond and Henrico County's health departments, Friday evening.

"We have not seen any significant increase in hospitalization [and] ventilator use is under 25%," Avula said during a news briefing. "It feels like the calm before the storm, and hopefully the storm will never come."

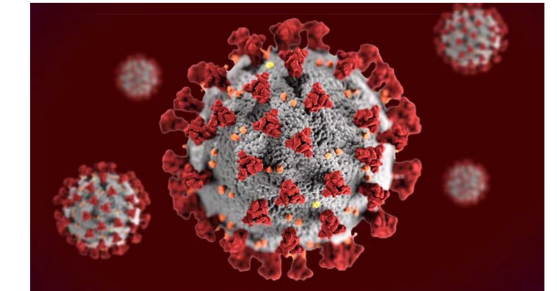
Examining the [University of Virginia's COVID-19 forecasting model](#), Avula said, Virginia seems



Dr. Danny Avula, director of Richmond and Henrico County health departments, at his April 17 news conference

Apr 21, 2020

Virginia hits pause on plans for 3 large field hospitals



COVID-19 (AP)
Updated: Apr. 21, 2020 at 5:52 PM EDT

U.S. Field Hospitals Stand Down, Most Without Treating Any COVID-19 Patients

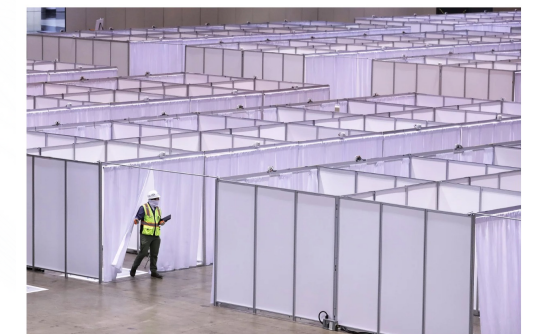
May 7, 2020 - 1:15 PM ET
Heard on All Things Considered

JOEL ROSE

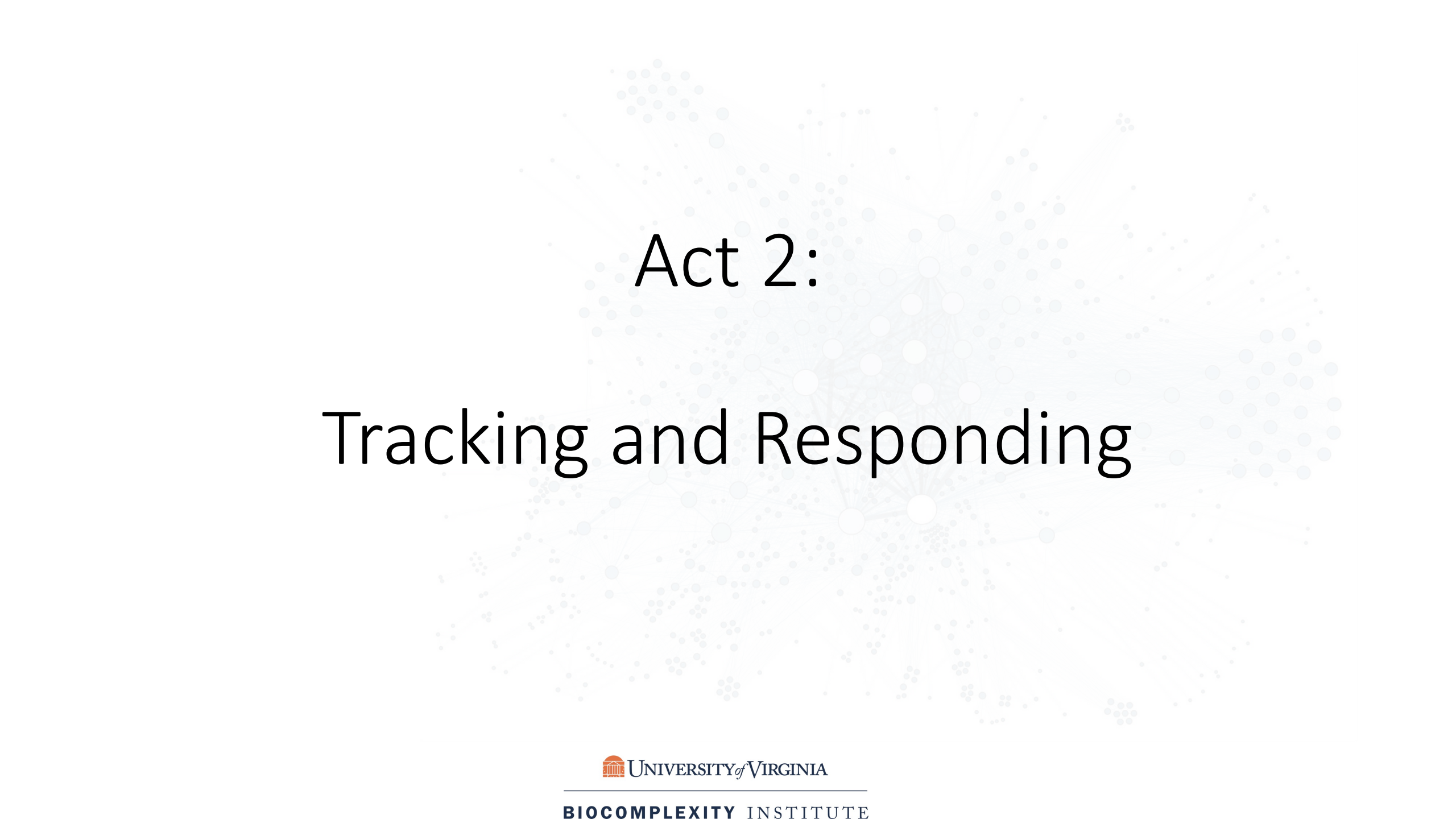
May 7, 2020

5-Minute Listen

PLAYLIST



Construction at the COVID-19 field hospital at McCormick Place in Chicago on April 10. The city pared back plans for a 3,000-bed temporary hospital at the nation's largest convention center as infection numbers decreased.

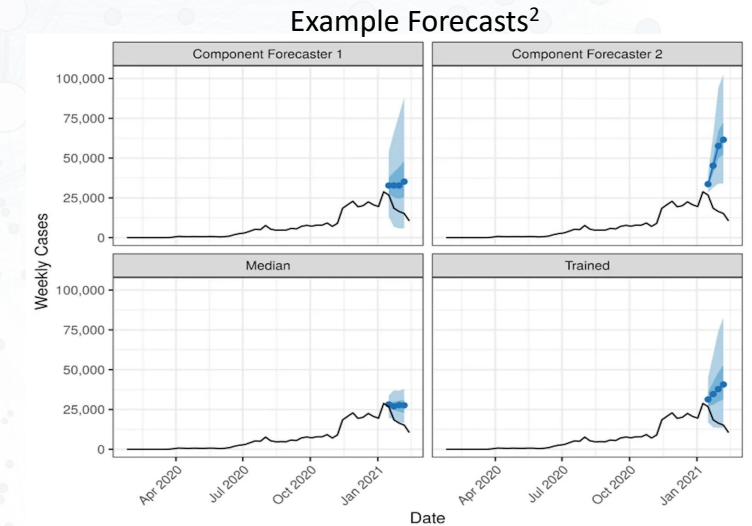
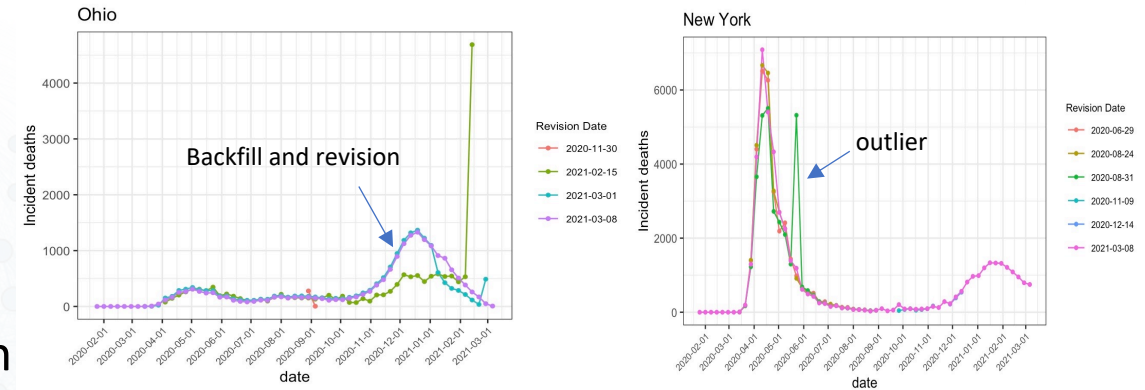
A complex network diagram with numerous nodes of varying sizes (small dots and larger circles) connected by thin lines, forming a dense, web-like structure that fills the background of the slide.

Act 2:

Tracking and Responding

Challenges in COVID-19 Forecasting

- Data – Reporting biases, backfill, outliers, etc.
 - Spatiotemporal heterogeneity in data reporting
 - Makes model training and evaluation a challenge
 - Multiple waves with varying peak sizes and duration
- Auxiliary data – covid-like illness, mask wearing, mobility, social distancing, surveys
 - Capture crucial population-level behavior
 - Nonlinear interactions with observed cases and hospitalizations
 - Hard to capture information flow from leading indicators to targets
- Teams have struggled to predict the onset, growth rate, peak size, and duration of the various waves²
 - Critical for medical resource allocation and planning



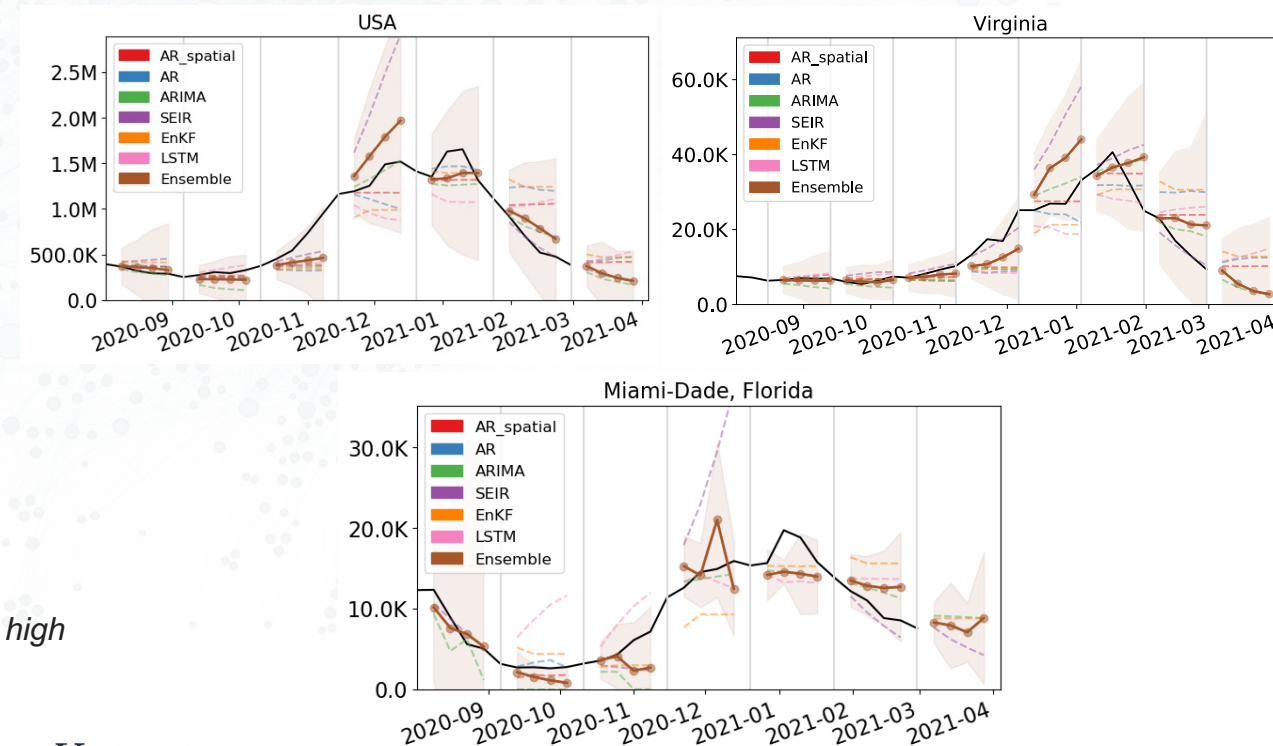
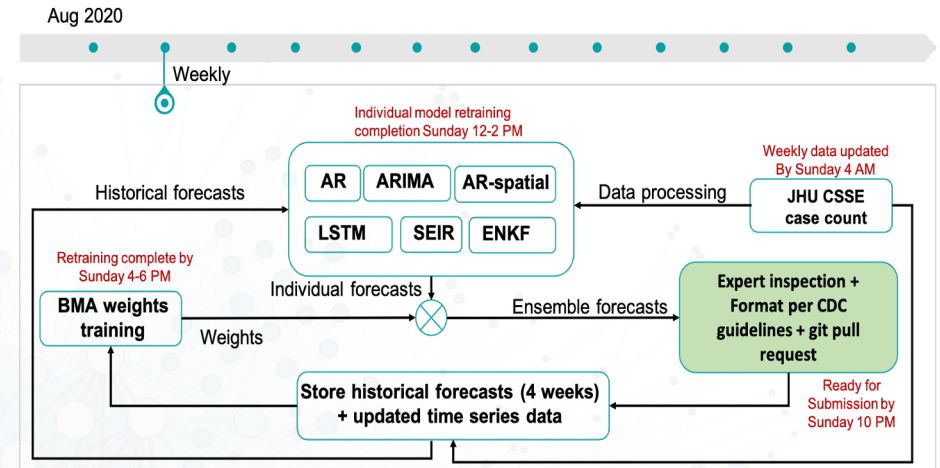
²Ray, E.; et al. 2021. "Challenges in training ensembles to forecast covid-19 cases and deaths in the United States." International Institute Forecasting

Ensemble Model (Aug 2020 –)

- Our model (UVA-Ensemble¹) – An ensemble of statistical, deep learning, and compartmental models (SEIR)
 - No single class of forecasting method is the best across horizons
 - Ensemble models are robust and the overall performance close to the best performing model
- Ensemble model – Bayesian model averaging (BMA)
 - A Gaussian Mixture Model likelihood

$$Pr(y|f_1, f_2, \dots, f_K) = \sum_k w_k g_k(y|f_k),$$

$w_k \rightarrow$ probability of model k being the best,
 $g_k \rightarrow$ Gaussian function mean f_k , std. dev. σ_k
 - w_k and σ_k estimated using EM algorithm
 - Models retrained every week with recent 6-week sliding window

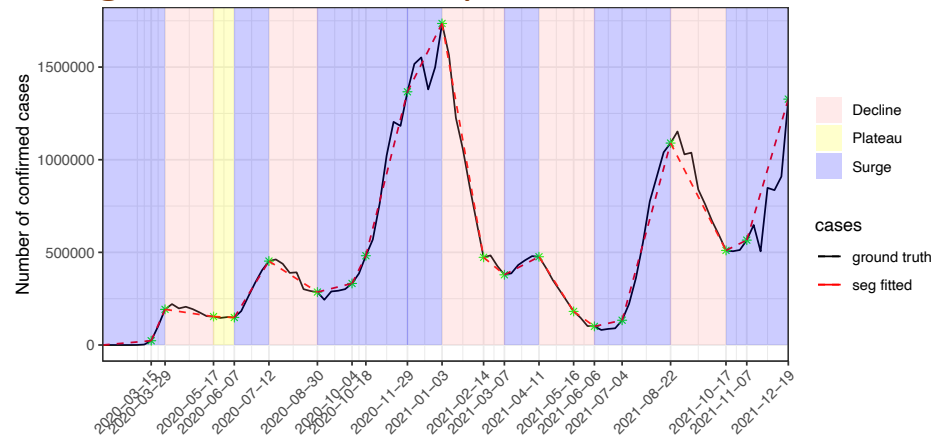


Adiga, Aniruddha, et al. "All models are useful: Bayesian ensembling for robust high resolution covid-19 forecasting." ACM SIGKDD 2021.

Phase Classification

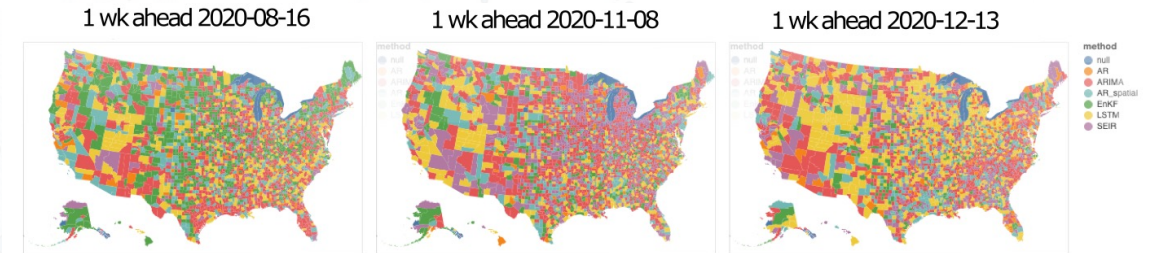
- Observation: Phase-dependent performance of individual models
 - Compartmental models effective in picking up growth/decline
 - Models like LSTMs can learn complex patterns across waves
 - Statistical methods perform well during the plateau phase
- Proposed Solution – Phase-Informed BMA
 - Training samples corresponding to a particular phase are employed to determine the weights
 - Phase classification: Given a time series $Y = \{y_1, y_2, \dots, y_T\}$ with time index set $\mathcal{T} = \{1, 2, \dots, T\}$, obtain a classifier $P_Y: \mathcal{T} \rightarrow \{S, D, P\}$

Segmentation based phase-classification

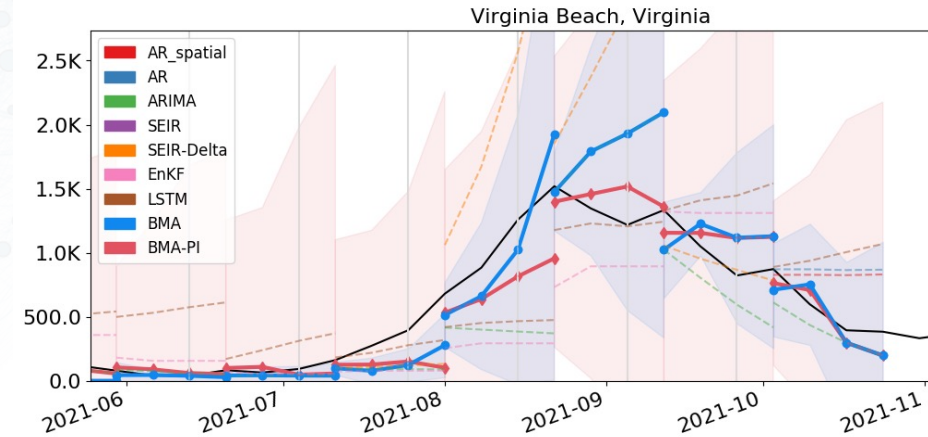


$$P_Y(t) = \begin{cases} S & \text{if } y_{b_i} > 1.1y_{b_{i-1}} \\ P & \text{if } 0.9y_{b_{i-1}} < y_{b_i} < 1.1y_{b_{i-1}} \\ D & \text{if } y_{b_i} < 0.9y_{b_{i-1}} \end{cases}$$

Different dominant models across counties



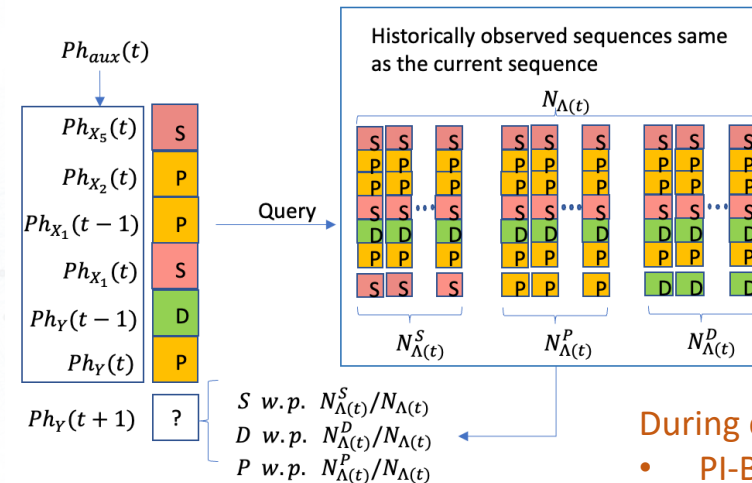
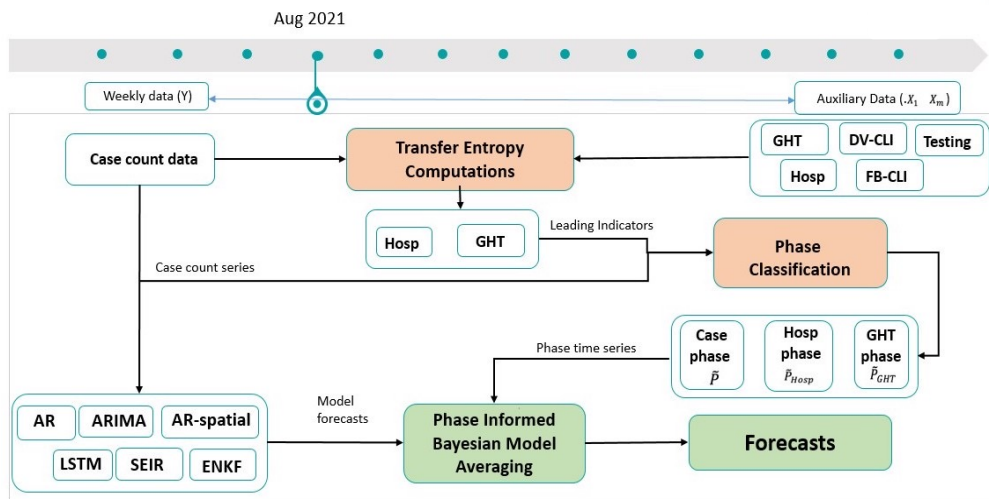
Improved forecasts by training phase-specific ensemble



Adiga, Aniruddha et al., "Phase-Informed Bayesian Ensemble Models Improve Performance of COVID-19 Forecasts", IAAI-23

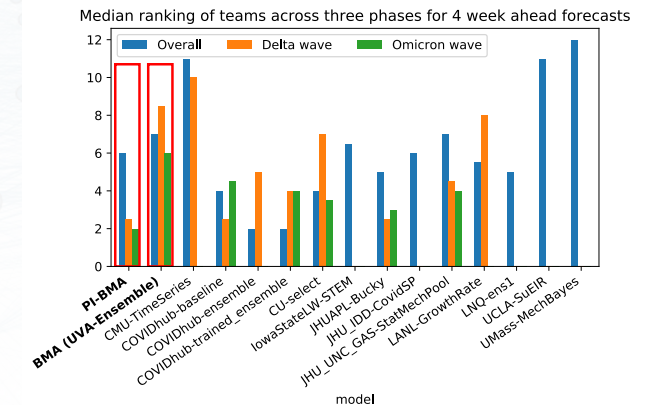
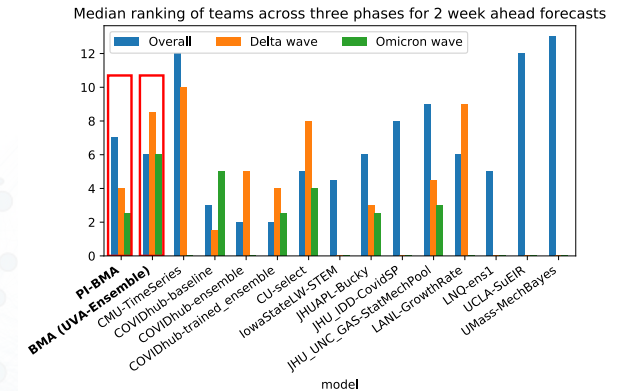
Phase Prediction

- Observation: Phase change can be predicted using auxiliary sources
- Step 1: Identify leading indicators with appropriate lags (using transfer entropy)
- Step 2: Apply temporal phase classification to individual signals
- Step 3: Use the historically observed phases to predict upcoming phase of target signal



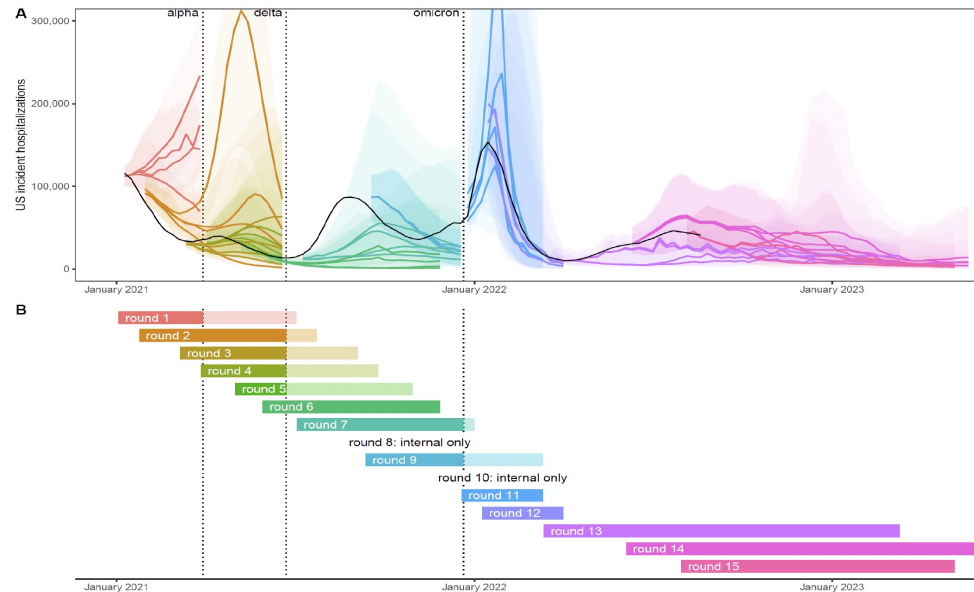
During critical phases:

- PI-BMA one of the top-ranking models - **Delta (2 out of 9) and Omicron (2 out of 6)**
- Provide considerably better forecasts compared to both BMA (UVA-Ensemble) and the rest of the forecast hub models



Adiga, Aniruddha et al., "Enhancing COVID-19 Ensemble Forecasting Model Performance Using Auxiliary Data Sources", IEEE Big Data 2022 (**Best Paper**)

National scenario projections (Dec 2020 -)



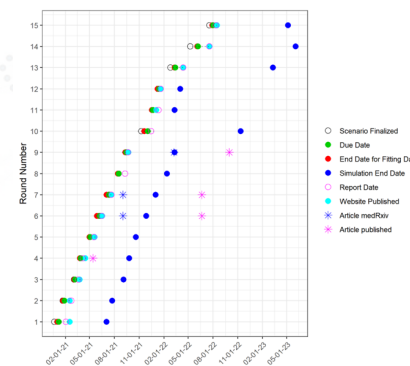
- ### Vaccine & NPIs
1. Vaccine supply and non-pharmaceutical interventions [Dec 2020]
 2. More transmissible variant (B.1.1.7) and NPIs [Jan 2021]
 3. Vaccine supply and NPIs [March 2021]
 4. Vaccine supply and NPIs [March 2021]
 5. Vaccine hesitancy and NPIs [May 2021]
 6. More transmissible variant and vaccine hesitancy [May 2021]
 7. Delta and vaccine uptake [July 2021]
 8. Immunologic waning [non-public practice round]

- ### Variants & Immunity
9. Childhood vaccination and hypothetical variant [Sept 2021]
 10. Boosters and waning [unreleased due to Omicron]
 11. Omicron 1, severity and transmission characteristics [Dec 2021]
 12. Omicron 2, severity and transmission characteristics [Jan 2022]
 13. Long term waning and variant [March 2022]
 14. Boosters and hypothetical variants [July 2022]
 15. Boosters and variants redux [August 2022]

Team Participation

	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
USC-SikAlpha															
UVA-adaptive															
JHU_IDD-CovidSP															
MOBS_NEU-GLEAM_COVID															
UNCC-hierbin															
UVA-EpiHiper															
JHUAPL-Bucky															
Karlen-pypm															
CU-AGE-ST															
NotreDame-FRED															
UTA-ImmunoSEIRS															
NCSU-COVSIM															
UF-ABM															
Total	5	5	4	6	8	9	9	8	8	7	8	9	8	7	7

Timeliness over 15 rounds



Scenario definitions from Round 11 (Omicron)	Higher immune escape / Lower transmissibility increase	Lower immune escape / Higher transmissibility increase
Lower severity: - Among naive individuals, 50% reduction in severity of Omicron infection, relative to Delta (all-age risk of hospitalization and death divided by two; age-specific risks at teams discretion). - Among previously infected or vaccinated, residual protection for Omicron cases: - Hospitalization: 85% [i.e., $\Pr(\text{hosp} \text{any immunity}) = 0.15 * \Pr(\text{hosp} \text{naive})$] - Death: 95% [i.e., $\Pr(\text{death} \text{any immunity}) = 0.05 * \Pr(\text{death} \text{naive})$] Status quo severity: - Among naive individuals, no change in severity of Omicron infection, relative to Delta - Among previously infected or vaccinated, residual protection for Omicron cases: - Hospitalization: 70% - Death: 85%	Advantage Omicron over Delta in South Africa, Rt ratio: 2.8 (Rt = 2.5) - Intrinsic transmissibility Omicron: 1x seasonally-adjusted R0 of Delta - Immune escape: 80% of previously immune are susceptible to infection Scenario A	Advantage Omicron over Delta in South Africa, Rt ratio: 2.8 (Rt = 2.5) - Intrinsic transmissibility Omicron: 1.66x seasonally-adjusted R0 of Delta* - Immune escape: 50% of previously immune are susceptible to infection Scenario B
	Scenario C	Scenario D

* Assuming Delta R0 = 6, Omicron R0 = 6 or R0 = 10

Images courtesy: Scenario Modeling Hub

Significant Public Health Impact



Early Release / Vol. 70

NPI decisions after primary vaccination (May 2021)

Morbidity and Mortality Weekly Report
May 5, 2021

Modeling of Future COVID-19 Cases, Hospitalizations, and Deaths, by Vaccination Rates and Nonpharmaceutical Intervention Scenarios — United States, April–September 2021

Rebecca K. Borchering, PhD^{1,*}; Cécile Viboud, PhD^{2,*}; Emily Howerton³; Claire P. Smith³; Shaun Truelove, PhD³;
Michael C. Runge, PhD⁴; Nicholas G. Reich, PhD⁵; Lucie Contamin, MS⁶; John Levander⁶; Jessica Salerno, MPH⁶;
Wilbert van Panhuis, PhD⁷; Matt Kinsey, PhD⁷; Kate Tallaksen, MS⁷; R. Freddy Obrecht, PhD⁷; Laura Asher, MPH⁷;
Cash Costello, MS⁷; Michael Kellogg⁷; Shelby Wilson, PhD⁷; Lauren Shier⁷; Molly E. Gallagher, PhD⁷; Luke C. Mullany, PhD⁷;
Kaitlin Rainwater-Lovett, PhD⁷; Joseph C. Lemaître, MS⁸; Juan Dent, ScM⁹; Kyra H. Grant⁹; Joshua Kaminsky, MS⁹; Stephen A. Lauer, PhD⁹;
Elizabeth C. Lee, PhD⁹; Hannah R. Meredith, PhD⁹; Javier Perez-Saez, PhD⁹; Lindsay T. Keegan, PhD⁹; Dean Karlen, PhD¹⁰; Matteo Chinazzi, PhD¹¹;
Jessica T. Davis¹¹; Kunpeng Mu¹¹; Xinyue Xiong, MSc¹¹; Ana Pastore y Piontti, PhD¹¹; Alessandro Vespignani, PhD¹¹; Ajitesh Srivastava, PhD¹²;
Przemyslaw Poretsky, PhD¹³; Sriniwas Venkatarayanan, PhD¹³; Aniruddha Adiga, PhD¹³; Bryan Lewis, PhD¹³; Brian Kuhn, MS¹³;
Joseph Outten¹³; James Schlitt, PhD¹³; Patrick Corbett¹³; Pyrrhos Alexander Tilonia, PhD¹³; Lijing Wang, MS¹³; Akhil Sai Peddireddy¹³;
Benjamin Hurt, MS¹³; Jianghuo Chen, PhD¹³; Anil Vulliamthi, PhD¹³; Madhav Marathe, PhD¹³; Jessica M. Healy, PhD¹⁴; Rachel B. Slayton, PhD¹⁴;
Matthew Biggerstaff, ScD¹⁴; Michael A. Johansson, PhD¹⁴; Kariona Shea, PhD¹⁴; Justin Lessler, PhD¹⁴

¹The Pennsylvania State University, State College, Pennsylvania; ²Fogarty International Center, National Institutes of Health, Bethesda, Maryland; ³Johns Hopkins Bloomberg School of Public Health, Baltimore, Maryland; ⁴U.S. Geological Survey, Laurel, Maryland; ⁵University of Massachusetts Amherst, Amherst, Massachusetts; ⁶University of Pittsburgh, Pittsburgh, Pennsylvania; ⁷Johns Hopkins University Applied Physics Laboratories, Laurel, Maryland; ⁸Ecole polytechnique fédérale de Lausanne, Lausanne, Switzerland; ⁹University of Utah, Salt Lake City, Utah; ¹⁰University of Victoria, Victoria, British Columbia, Canada; ¹¹Northeastern University, Boston, Massachusetts; ¹²University of Southern California, Los Angeles, California; ¹³University of Virginia, Charlottesville, Virginia; ¹⁴CDC COVID-19 Response Team

Expansion of vaccine eligibility to 5-11-year-olds (Sep 2021)

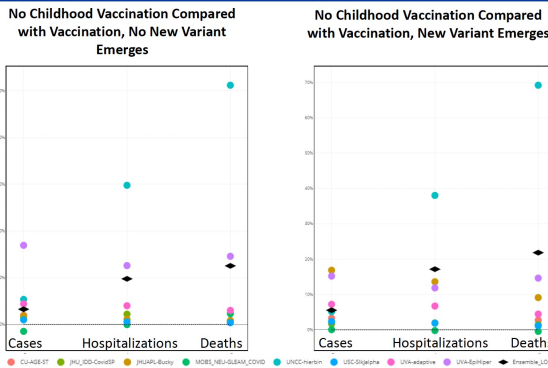
Projected outcomes averted with childhood vaccination (September 2021–March 2022)

“No New Variant” Scenarios

- Vaccination of 5-11-year-olds was projected to reduce cases, hospitalizations, and deaths between 3 and 13% (point estimates over entire projection period)
- Wide variability between individual projections and working to visualize uncertainty

“New Variant” scenarios

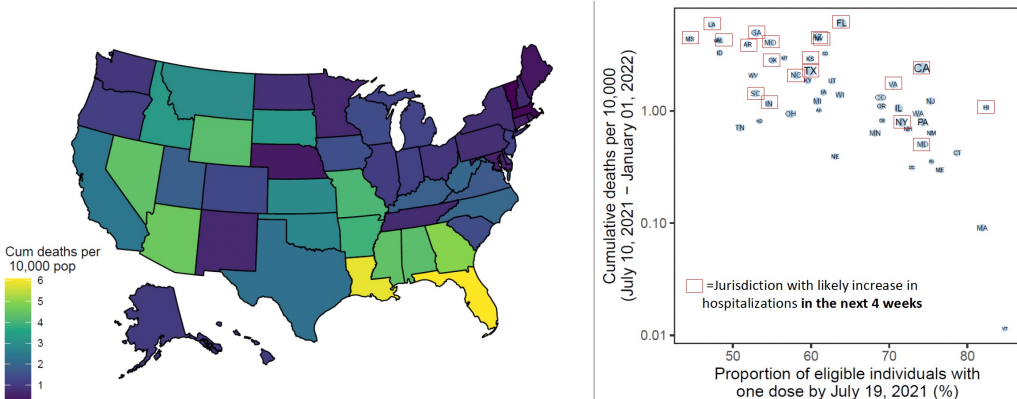
- Estimated reductions due to vaccination greater than when compared to the “No Variant” Scenario



Slide courtesy: Matt Biggerstaff, CDC

Potential impact of Delta wave across states (Jul 2021)

Projected cumulative deaths, Jul 4, 2021–Jan 1, 2022, low vaccine/high transmissibility scenario

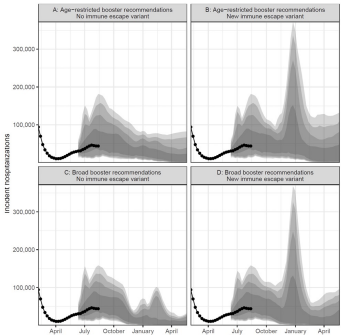


Slide courtesy: Matt Biggerstaff, CDC

Role in bivalent dose recommendation (Sep 2022)

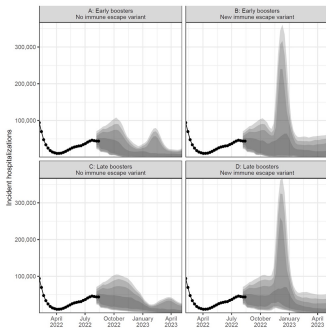
Round 14: National ensemble projection intervals - Hospitalizations

Round 14
Regardless of presence of a new variant, flu-like vaccine uptake in individuals ages ≥18 years would lead to a
>20% reduction in hospitalizations and
>15% reduction in deaths versus a recommendation for individuals ages ≥50 years only



Round 15: National ensemble projection intervals - Hospitalizations

Round 15
Absent a new variant, boosters to individuals ages ≥18 years in **September** could prevent
137,000 more hospitalizations¹ and
9,700 more deaths² compared to boosters in **November**

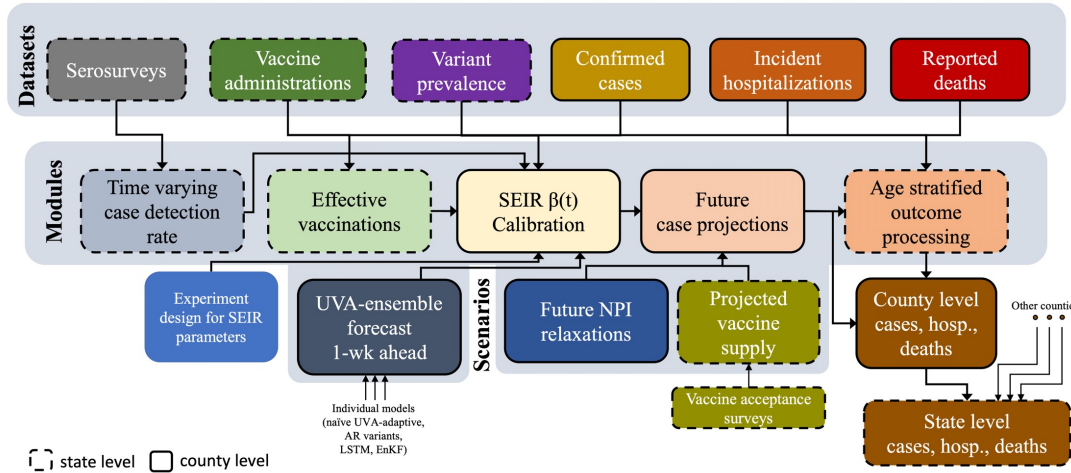


<https://www.cdc.gov/vaccines/acip/meetings/downloads/slides-2022-09-01/08-covid-oliver-508.pdf>



Our approach (1) – Tiered Multi-strain modeling

Base framework integrates vaccine, NPI, outcomes data for calibration



Translating neutralization studies into model parameters

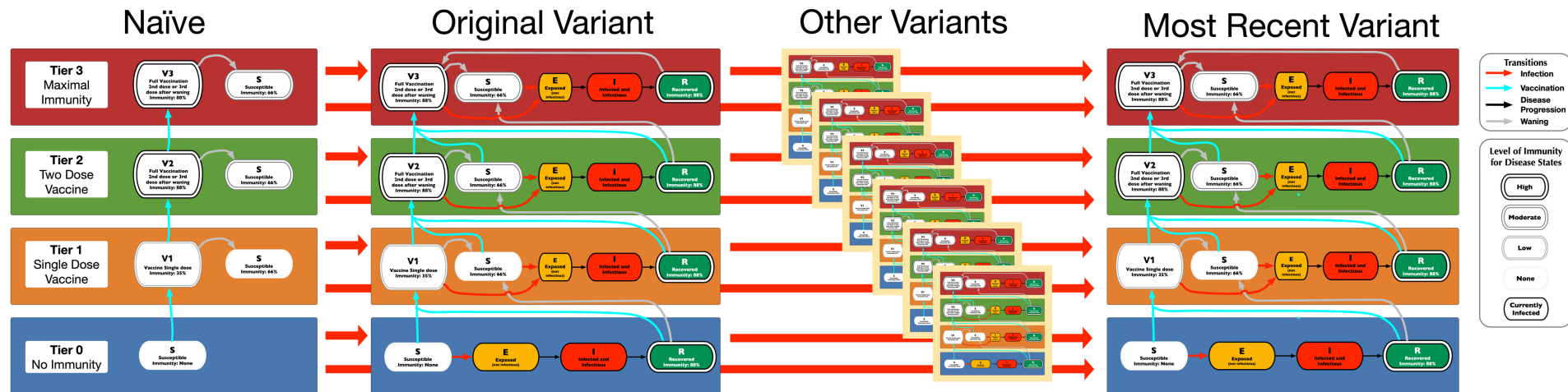
Vaccine Efficacy

	1st dose	2nd dose	booster	reformulated booster
pre-Omicron	0.35	0.884	0.935	0.8
Omicron	0.07	0.1768	0.67	0.8
X	0.07	0.1768	0.48	0.48

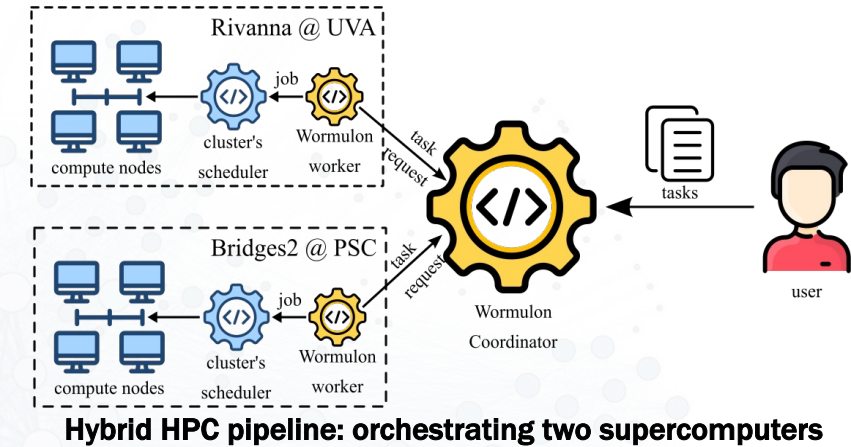
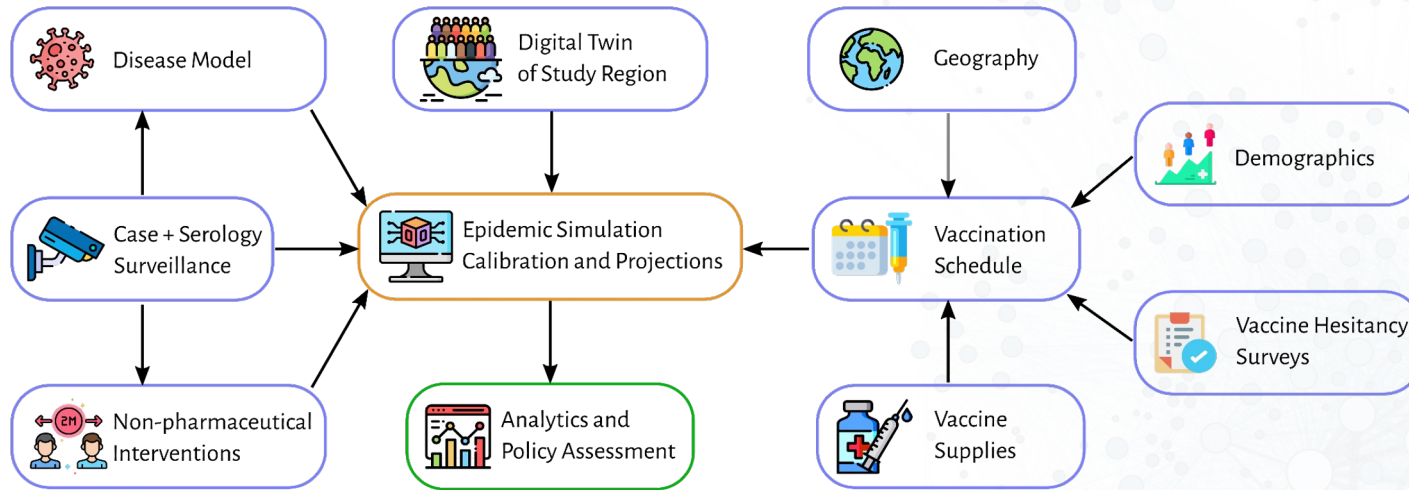
Immuno-Escape

	preomicron	BA.1	BA.2	BA.2.12	BA.4/5	X
prior infection						
naïve	1	1	1	1	1	1
preomicron	0	0.8	0.8	0.8	0.8	0.8
BA.1	0	0	0.3	0.6	0.8	0.8
BA.2	0	0	0	0.4	0.7	0.8
BA.2.12	0	0	0	0	0.5	0.7
BA.4/5	0	0	0	0	0	0.4
X	0	0	0	0	0	0

Tiered immunity and variant representation



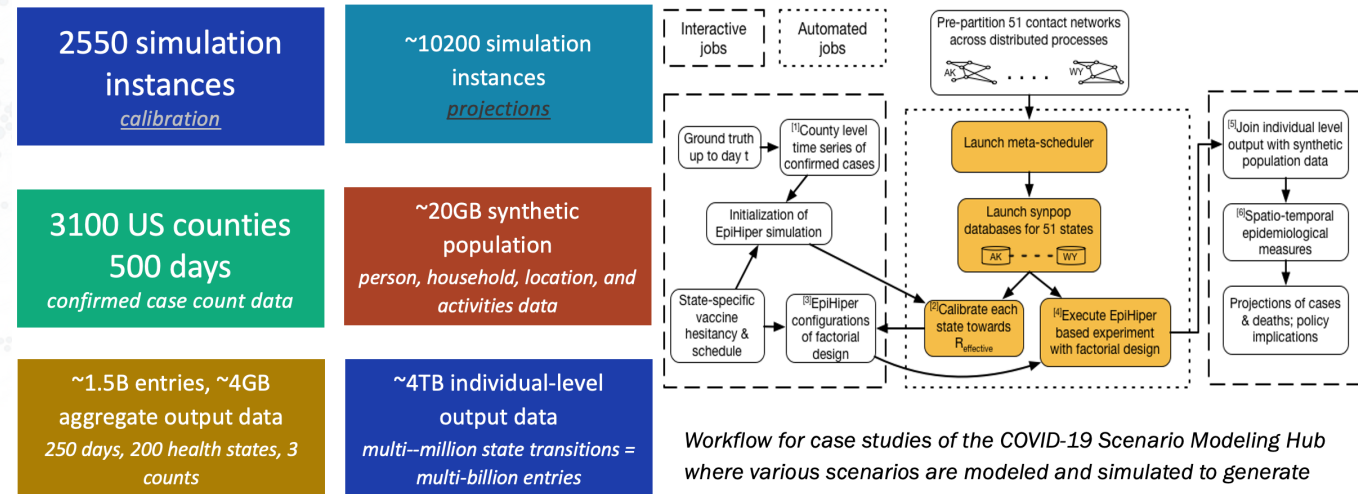
Our approach (2) – Digital twin representation



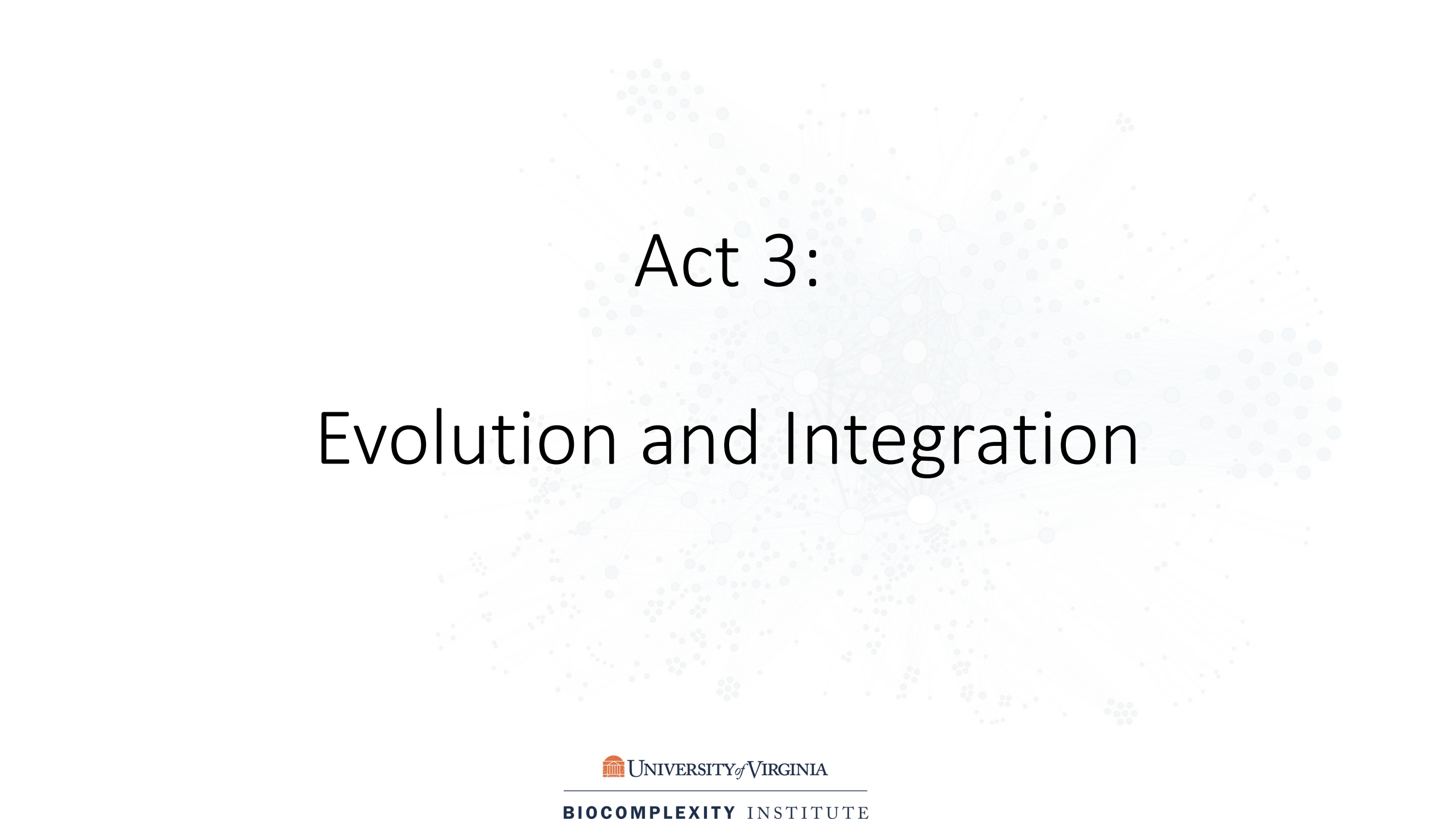
Data intensive HPC end-to-end workflow

Bhattacharya, Parantapa et al. "Data-Driven Scalable Pipeline using National Agent-Based Models for Real-time Pandemic Response and Decision Support". *The International Journal of High-Performance Computing Applications (IJHPCA)*, 2022.

Finalist, 2021 ACM Gordon Bell Special Prize for HPC COVID-19 Research



Workflow for case studies of the COVID-19 Scenario Modeling Hub where various scenarios are modeled and simulated to generate projections of cases, hospitalization, and deaths in the US at national and state levels.

A complex network diagram with numerous nodes of varying sizes (small dots and larger circles) connected by thin lines, forming a dense, web-like structure that fills the background of the slide.

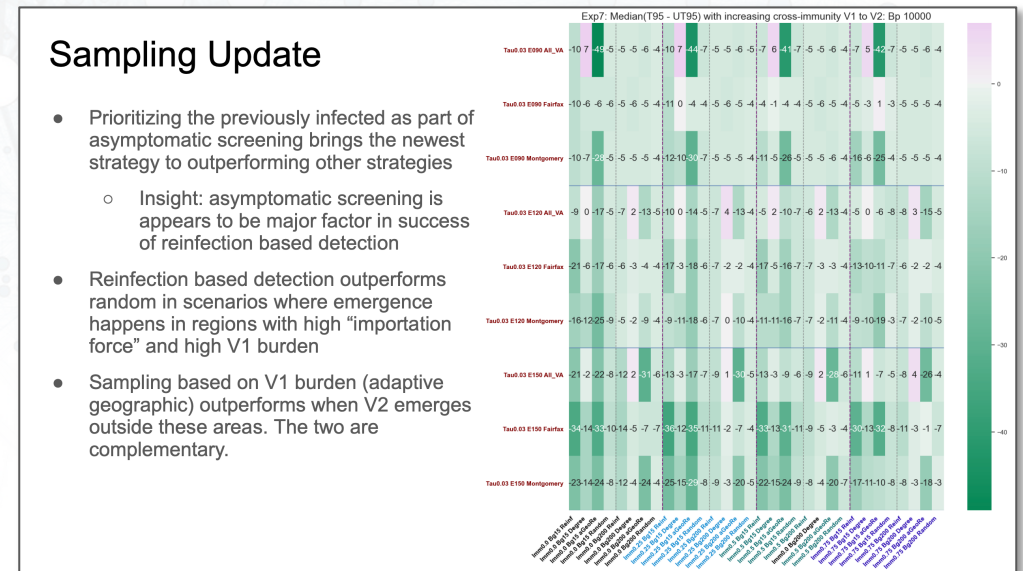
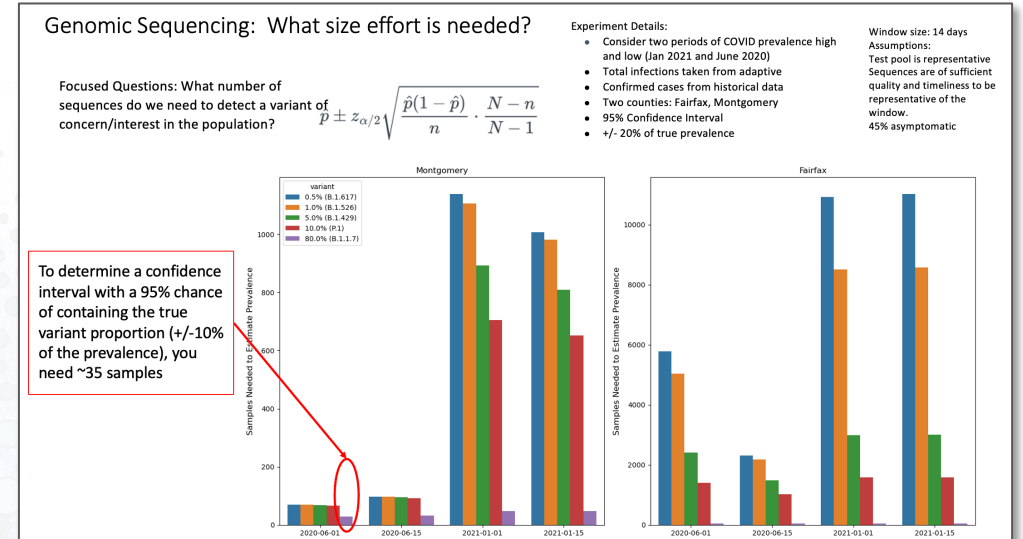
Act 3:

Evolution and Integration

Genomic Surveillance

**Questions: What variants are next?
How many sequences do we need to
have warning time on the emergence of
these new variants?**

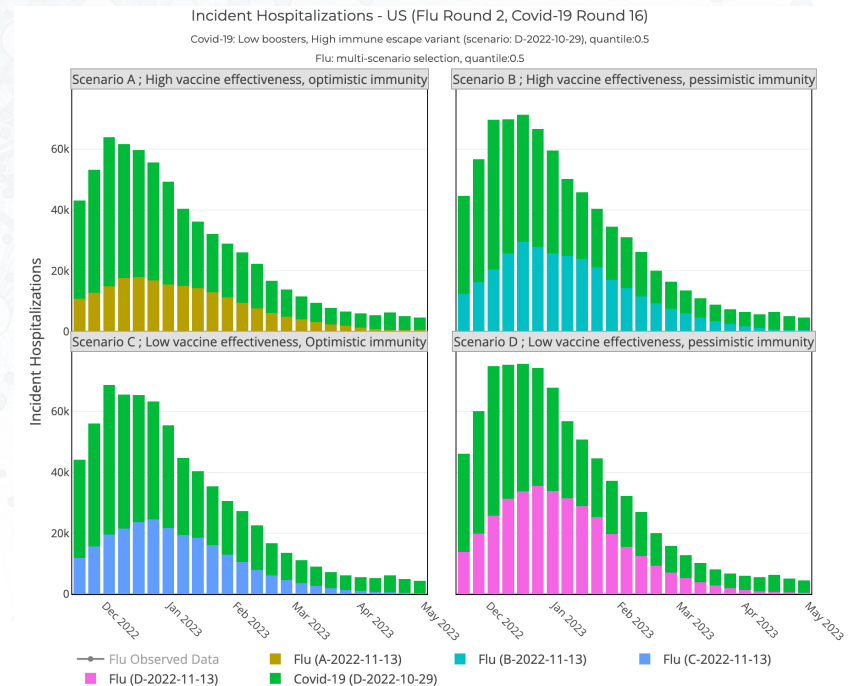
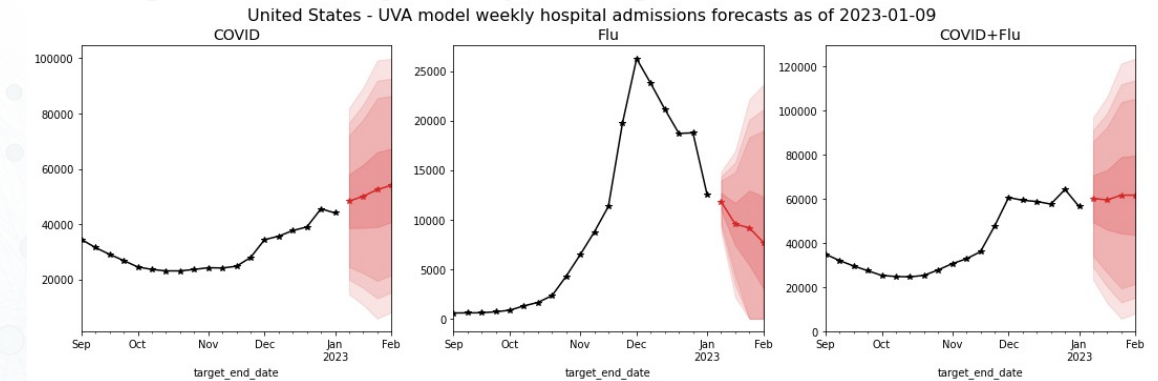
- Addressed with simple analytic approaches
- Evaluated different heuristic and adaptive sampling strategies within an agent-based model with different seedings of novel variants (how to get more bang for your buck)



COVID and Other Respiratory Diseases

Question: What does this winter look like with COVID and Influenza?

- Repurposing existing pipelines for Influenza focused forecasting and scenario modeling Hubs
- Combined healthcare burden across respiratory diseases
- Interaction between co-evolving pathogens (due to behavioral adaptations, surveillance challenges) is unclear



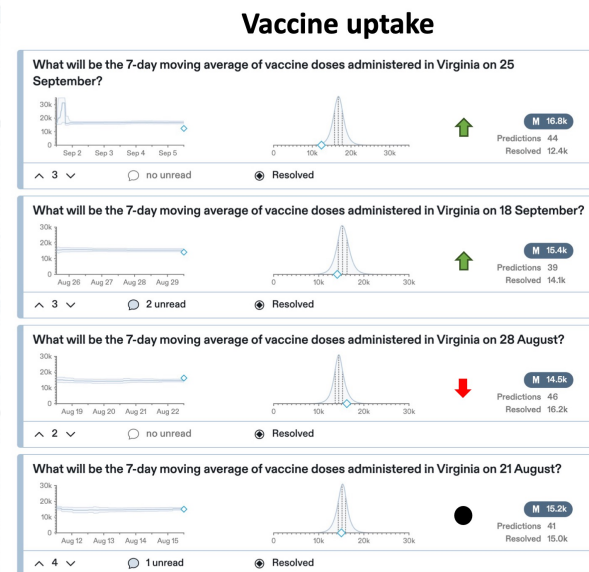
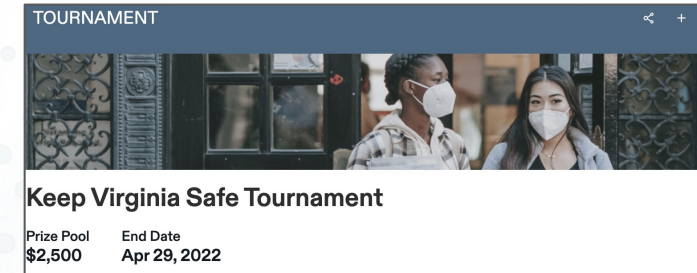
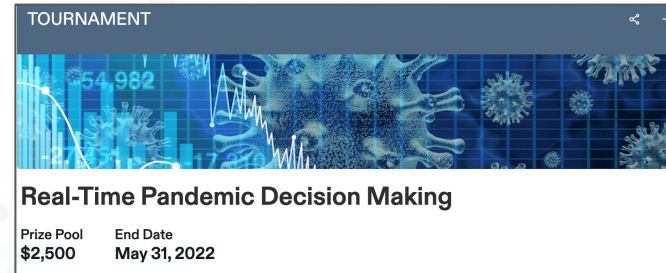
Courtesy: <https://fluscenariomodelinghub.org/>

Incorporating Human Judgement

Question: How to use human forecasting systems to improve forecasts and projections?

- Partnered with Metaculus Inc.
- Multiple tournaments hosted
- Questions about direct metrics (e.g., cases) but also about scenario shaping elements (e.g., vaccination)

Screenshots from: <https://www.metaculus.com/>



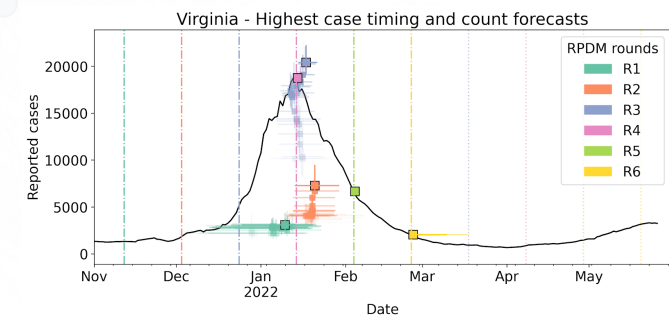
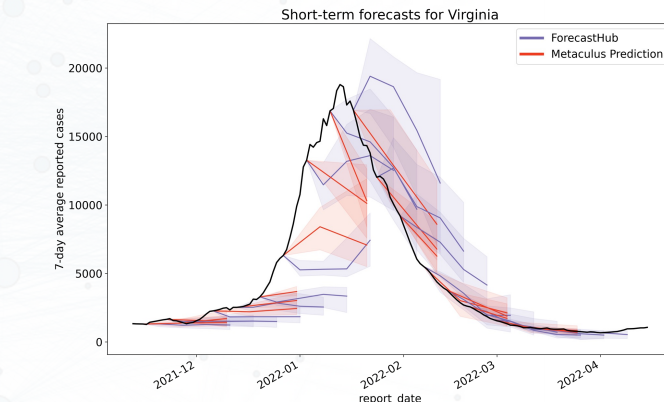
Sept 25

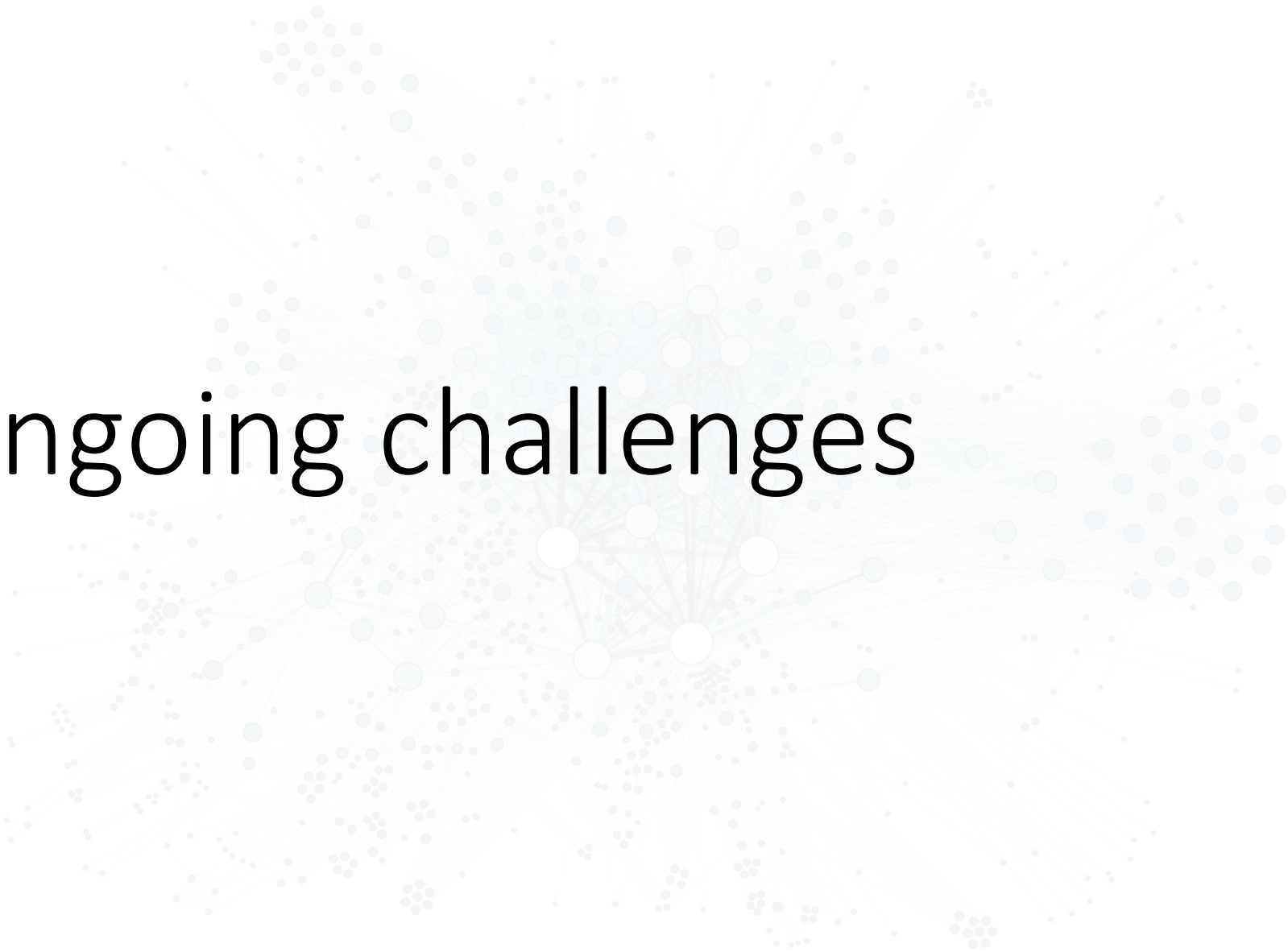
Sept 18

Aug 28

Aug 21

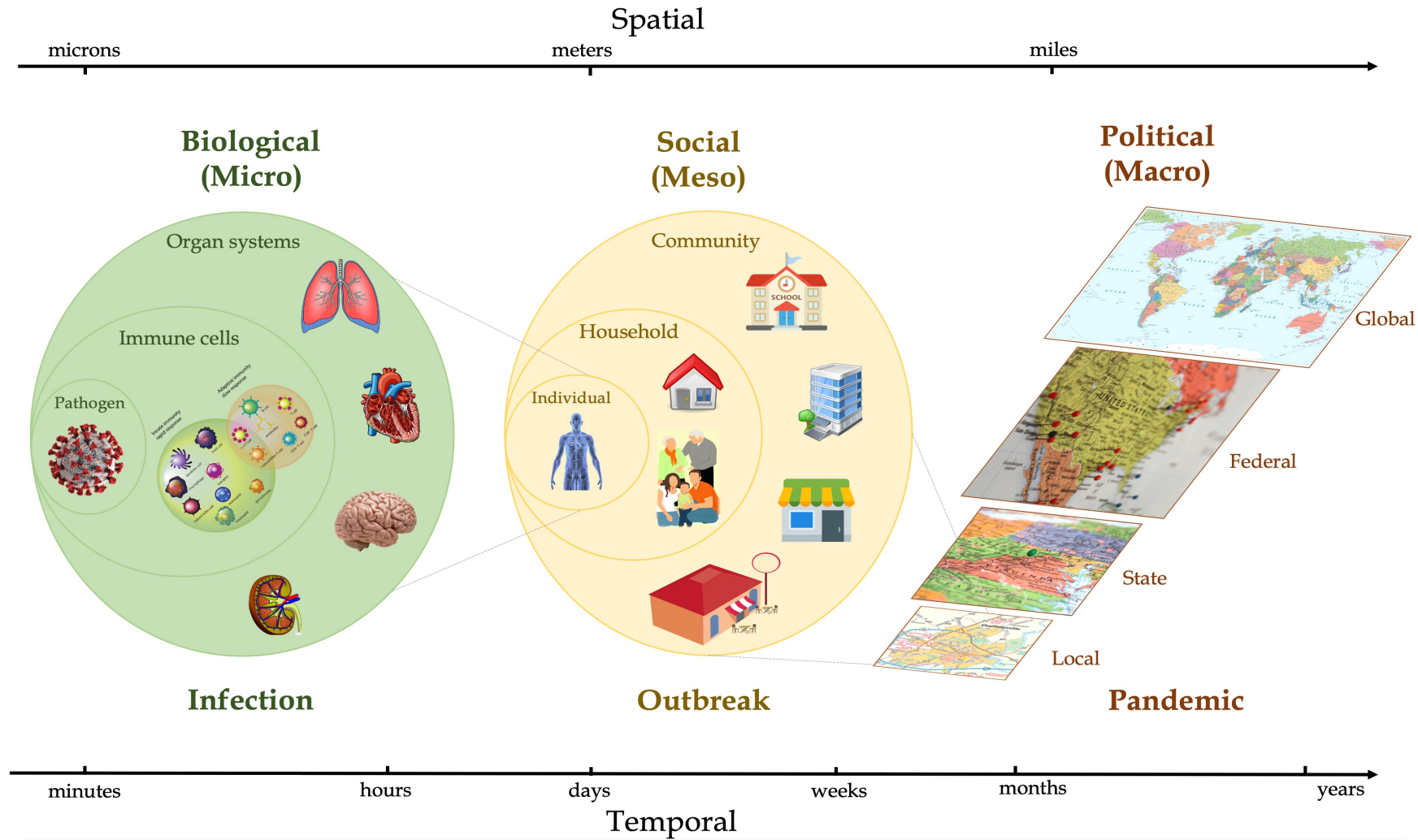
After initial underprediction, more optimistic about vaccine uptake during September.





Ongoing challenges

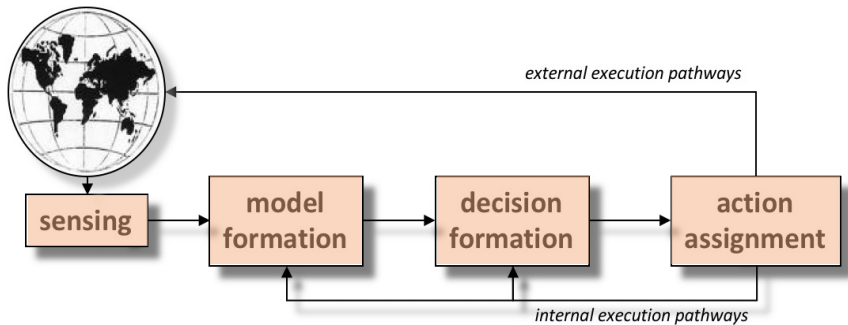
Multi-scale modeling



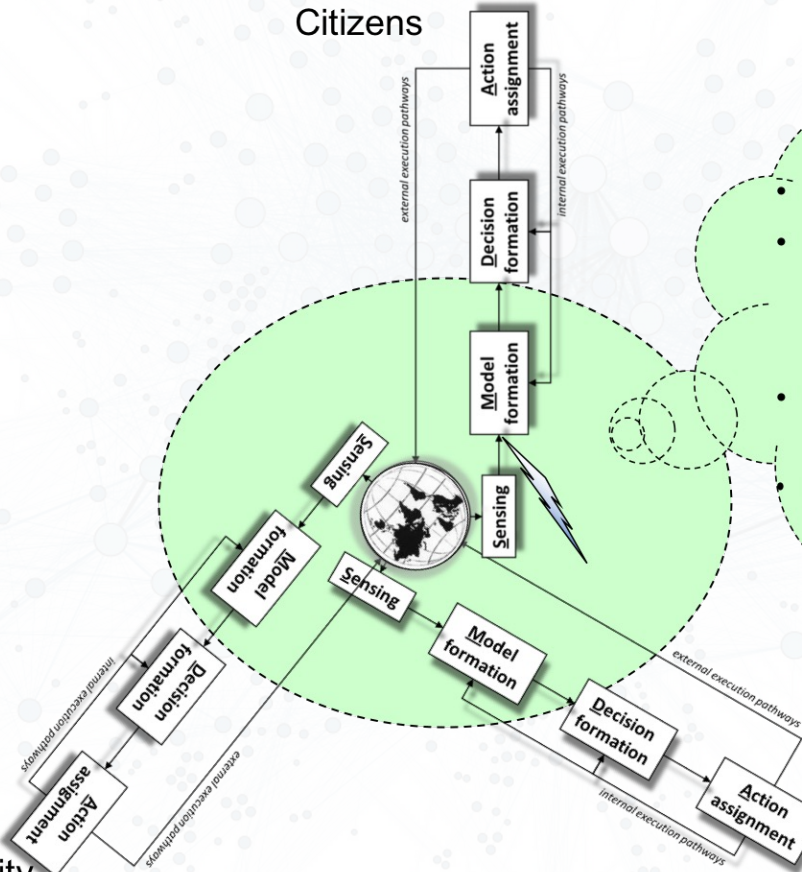
Need for capturing heterogeneity via multi-scale, multi-theory, multi-level network representations

Decentralized decision making

Context-specific, decentralized information seeking and decision making across socio-political scales



US, State &
Local Authority



- 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

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

Computing challenges

Computational Intractability:

Basic problems are computationally challenging (often #P-hard); HPC simulations are not optional

BigData Requirements:

330 million people and 12.6 billion interactions/day between individuals. Diverse real-time data streams

Availability of computing resources:

Computing resources are needed for sustained periods possibly unknown durations – machines fail, need maintenance and need to be shared

Variability and experimental design:

Multiple replicates needed to understand variability and multiple cells needed for a full design

Real-time requirements:

Results must be timely -- the clock starts as soon as the question is posed, and the base datasets/codes need to be updated

Operational challenges



Need: New approaches for Validation & Verification, Uncertainty Quantification for ensuring model adequacy and building trust



The science behind COVID-19 COVID-19 Conflict & humanitarian

The stark reality of how COVID-19 has worsened global inequality

The toll of the pandemic has been hardest on the most vulnerable, pushing millions into poverty and leaving them more at risk of disease, hunger and violence.

29 June 2022 • 4 min read • by [Ezra Joli](#)



VIEWPOINT | VOLUME 9, 100232, MAY 01, 2022

Looking back and moving forward: Addressing health inequities after COVID-19

Kimberlyn McGrail • [Jeffrey Morgan](#) • [Arjumand Siddiqi](#)

[Open Access](#) • Published: March 16, 2022 • DOI: <https://doi.org/10.1016/j.lana.2022.100232> • [Check for updates](#)

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Summary

We will likely look back on 2020 as a turning point. The pandemic put a spotlight on existing societal issues, accelerated the pace of change in others, and created some new ones too. For example, concerns about inequalities in health by income and race are not new, but they became more apparent to a larger number of people during 2020. The speed and starkness of broadening societal conversation, including beyond the direct effects of COVID-19, create an opportunity and motivation to reassess our understanding of health. Perhaps more importantly, it is an opportunity to reduce inequities in who has access to who

Need: New approaches for addressing challenges in governance, ethics, logistics, diplomacy and one health

Key takeaways

- Ensembling approaches prevail over others
- Theory guided Data science (TGDS) bridges the domain experts and data scientists
- Human in the loop is unavoidable. Wisdom of (expert) crowds.
- Data summarization (visualizations) is key to make decisions (or even make sense of the data)
- Team Science is essential to address real-world problems. Rethinking credit sharing practices.
- Open-source environment (papers, code, data) accelerates research and ensures reproducibility. Incentive mechanisms!
- Automated pipelines must be built with scalability, robustness, development and testing in mind.
- Translational research: Start from the problem. Not from the data. From papers to practice.

Questions?

Biocomplexity Institute: <https://biocomplexity.virginia.edu/>

COVID-19 Response: <https://nssac.github.io/covid-19/>

Email: srini@virginia.edu

Twitter: @sriniv_venkat