ORAN: A meta-modeling platform to drive real-life and online outbreak simulations

UMass Graduate School of Biomedical Sciences
25th Annual Research Retreat

ORAN:

A meta-modeling framework to drive real-life and online outbreak simulations

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UMASS MEDICAL SCHOOL

(A very short intro about myself and Co-Labo)

1998-2002
UNS Argentina
PhD in Mathematics

2002 - 2005
University of Chicago
Postdoc

2007-2009
University of Los Angeles
MFA Design Media Arts

2011 - 2015
Harvard & Fathom
Data visualization researcher

2016-2020
Broad Institute
Computational scientist

2020-
UMass Medical School
Data visualization researcher

The Colubri Laboratory (co-labo) will focus on digital epidemiology, data visualization, machine learning and mobile tools

https://co-labo.org

ALBERT CAMUS

LA PESTE

nrf

GALLIMARD

COVID-19 Dashboard by the Center for Systems Science and Engineering (CSSE) at Johns Hopkins University (JHU)

Global Cases
43,438,043

Cases by Country/Region/Sovereignty

8,699,321	US
7,909,959	India
5,409,854	Brazil
1,520,800	Russia
1,209,651	France
1,102,301	Argentina
1,098,320	Spain
1,025,052	Colombia
897,740	United Kingdom
891,160	Mexico
888,715	Peru
716,759	South Africa
574,856	Iran
542,789	Italy
503,598	Chile

Admin0

Last Updated at (M/D/YYYY)
10/26/2020 9:24 PM

Cumulative Cases | Active Cases | Incidence Rate | Case-Fatality Ratio | Testing Rate

189
countries/regions

Lancet Inf Dis Article: Here. Mobile Version: Here. Data sources: Full list. Downloadable database: GitHub, Feature Layer.
Lead by JHU CSSE. Technical Support: Esri Living Atlas team and JHU APL. Financial Support: JHU, NSF, Bloomberg Philanthropies and Stavros Niarchos Foundation. Resource support: Slack, Github and AWS. Click here to **donate** to the CSSE dashboard team, and other JHU COVID-19

Global Deaths
1,158,596

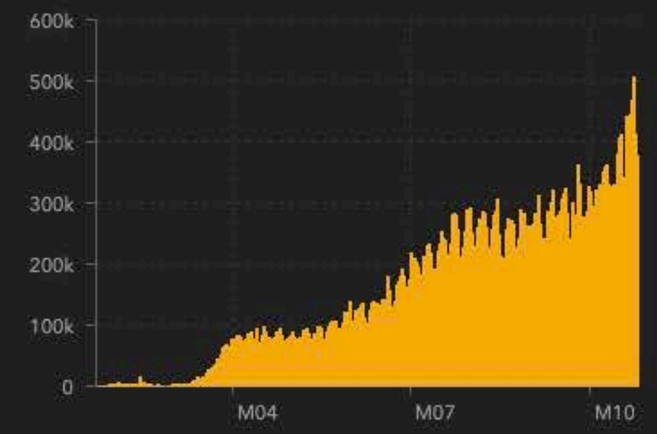
225,689 deaths	US
157,397 deaths	Brazil
119,014 deaths	India
88,924 deaths	Mexico
45,088 deaths	United Kingdom
37,479 deaths	Italy
35,052 deaths	France

Global Deaths

US State Level
Deaths, Recovered

33,424 deaths, 79,162 recovered	New York US
17,975 deaths, 758,192 recovered	Texas US
17,386 deaths, recovered	California US
16,449 deaths, recovered	Florida US
16,292 deaths, 36,545 recovered	New Jersey US
9,881 deaths, 122,856 recovered	

US Deaths, Rec...



Daily Cases

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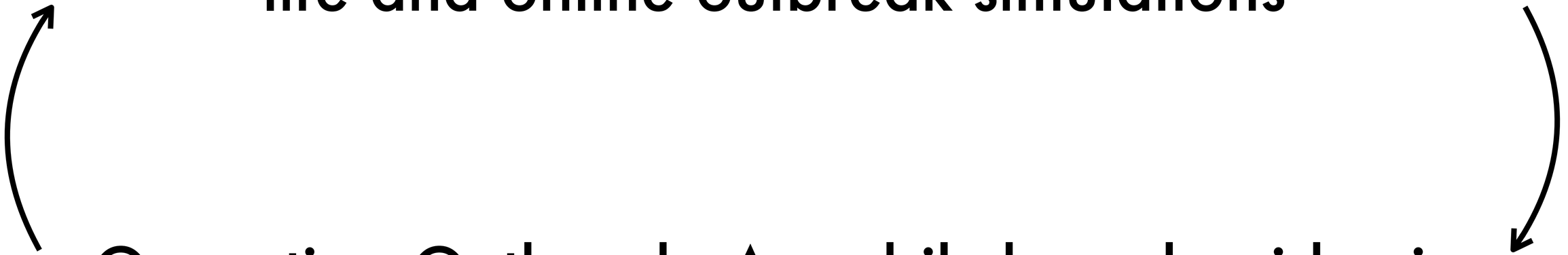
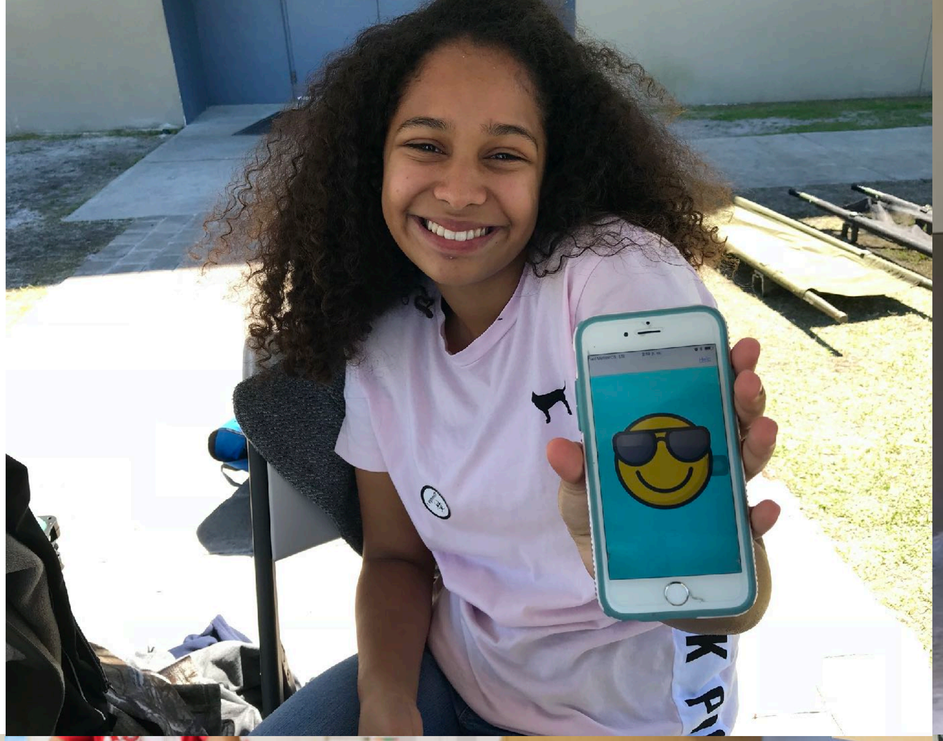


Operation Outbreak: A mobile-based epidemic simulation platform

OPERATION OUTBREAK



What's Operation Outbreak?

OO is a agent-based epidemic simulation platform, where the "agents" are real people using a custom app to simulate spread of a virtual pathogen within a population

https://operationoutbreak.org

It began in 2015 at Sarasota Military Academy as a two-week infectious diseases curriculum for middle schoolers culminating in a mock outbreak exercise

Outbreak exercises are not new

Board and computer games: ***Pandemic***, ***Plague Inc***

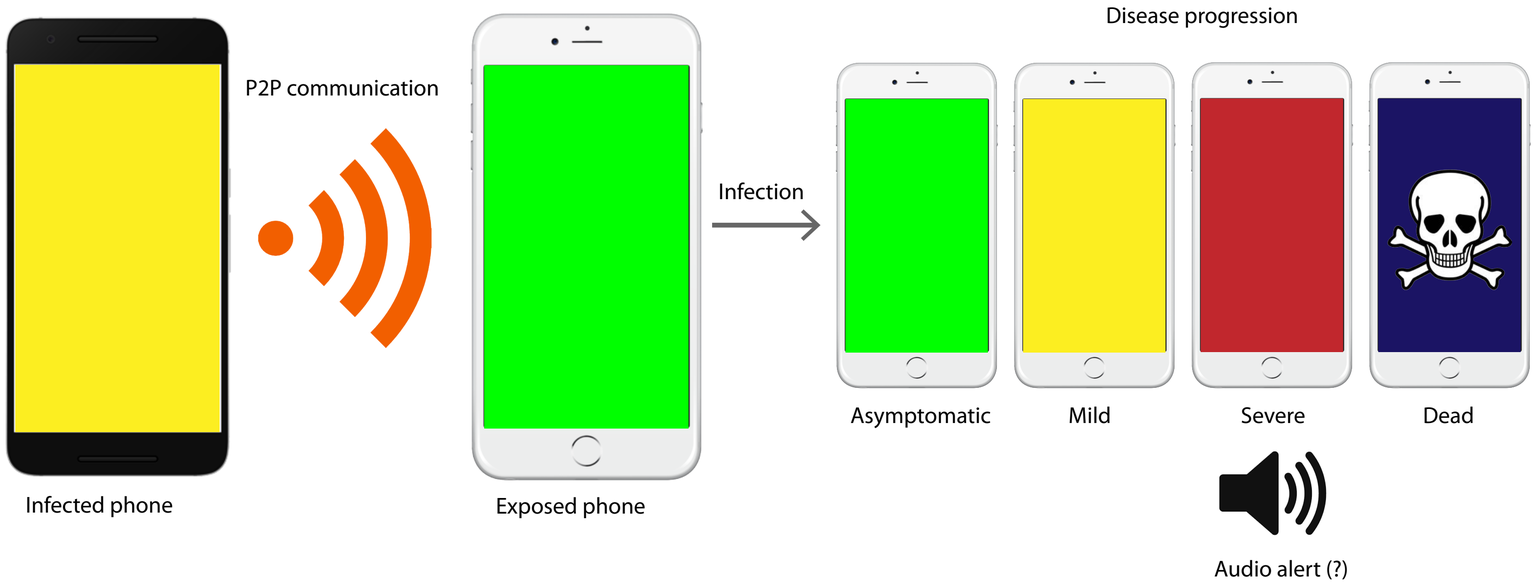
Crimson Contagion: Simulation of an influenza pandemic, run by the Department of Health and Human Services in 2019. Predicted that the US would be underfunded, underprepared and too disorganized to deal with a global pandemic.

'Virtual outbreaks designed and implemented with public-health studies in mind have the potential to bridge the gap between traditional epidemiological studies on populations and computer simulations, involving both ***unprogrammed human behavior*** *and* ***large numbers of test participants*** *in a controlled environment where the* ***disease parameters are known****."*

The untapped potential of virtual game worlds to shed light on real world epidemics. Lofgren ET, Fefferman, NH. *The Lancet Infectious diseases* (2007)

An app-based outbreak simulation

After I learned about the SMA mock outbreak exercise, I suggested that a digital pathogen could be transmitted over Bluetooth, imitating some of the infection characteristics of a real pathogen



Initial sketches

First app-based simulation at SMA in 2018 (Ebola outbreak)

$P_{sick}=0.6$

$P_{v.sick}=0.4$

$P_{sick→rec}=0.5$

$P_{sick→dead}=0.5$

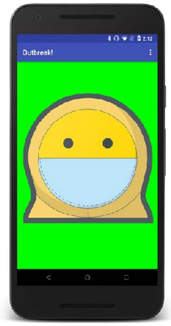
$P_{v.sick→rec}=0.1$

$P_{v.sick→dead}=0.9$

$P_{infect}=0.002$

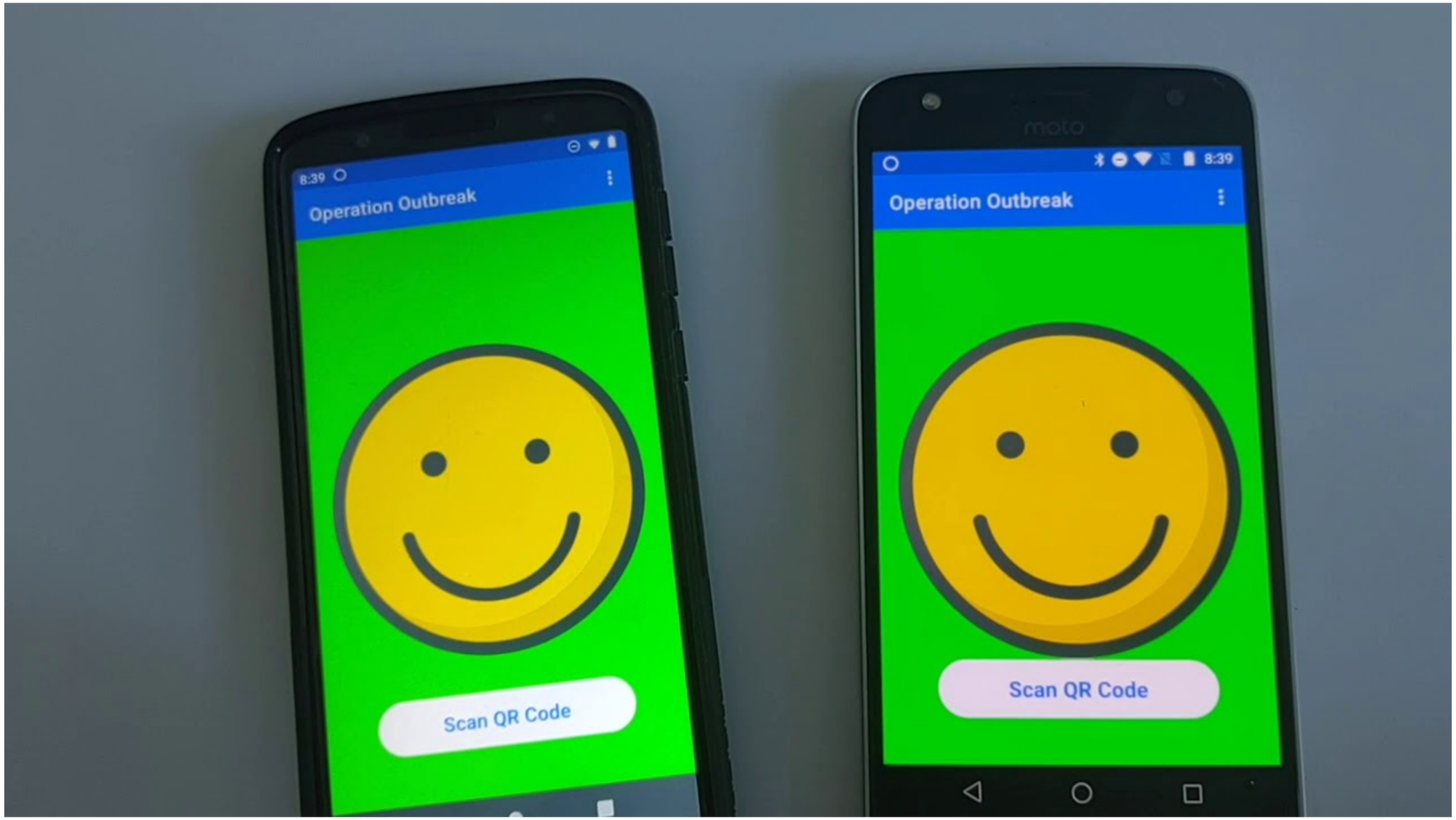
$T_{asym}=20$ min

$T_{sym}=10$ min



Bluetooth Low Energy (BLE) beacon

Demo video of the OO app

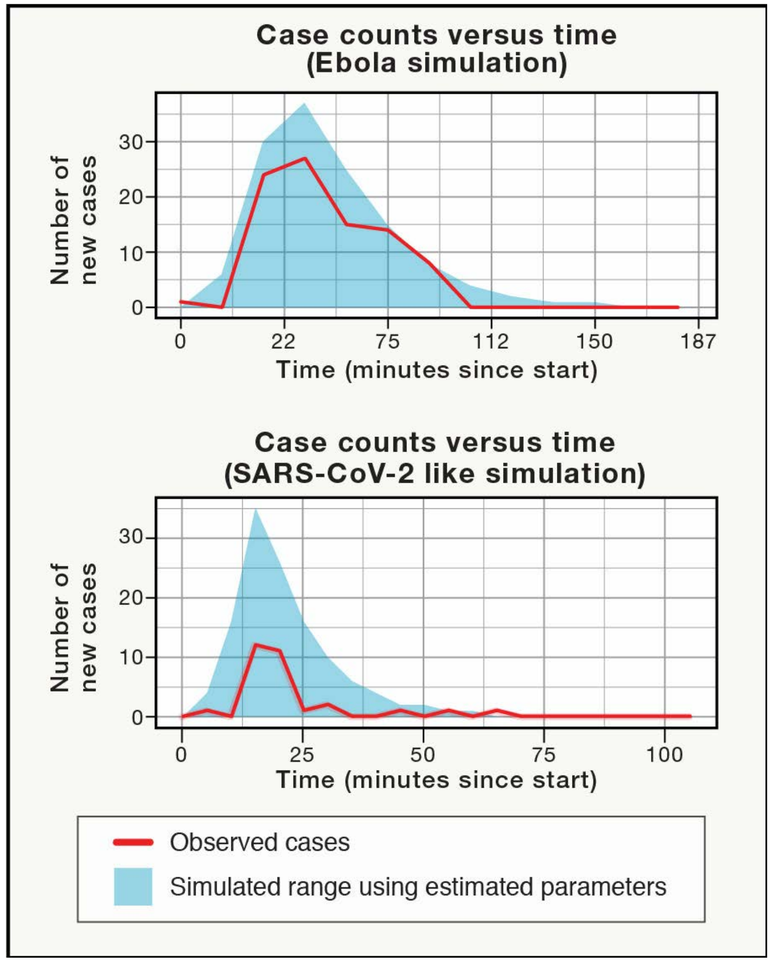


SARS-like OO simulations

In early December 2019, we simulated outbreaks of the SARS-like virus at SMA (185 participants) and the annual retreat of the Broad Institute of MIT and Harvard (100 participants).

We also simulated this virus in February 2020 at the day-long Florida Undergraduate Research Conference (FURC); 260 of the 590 attendees installed the app to run an unsupervised simulation for the full conference.

Some results from these simulations



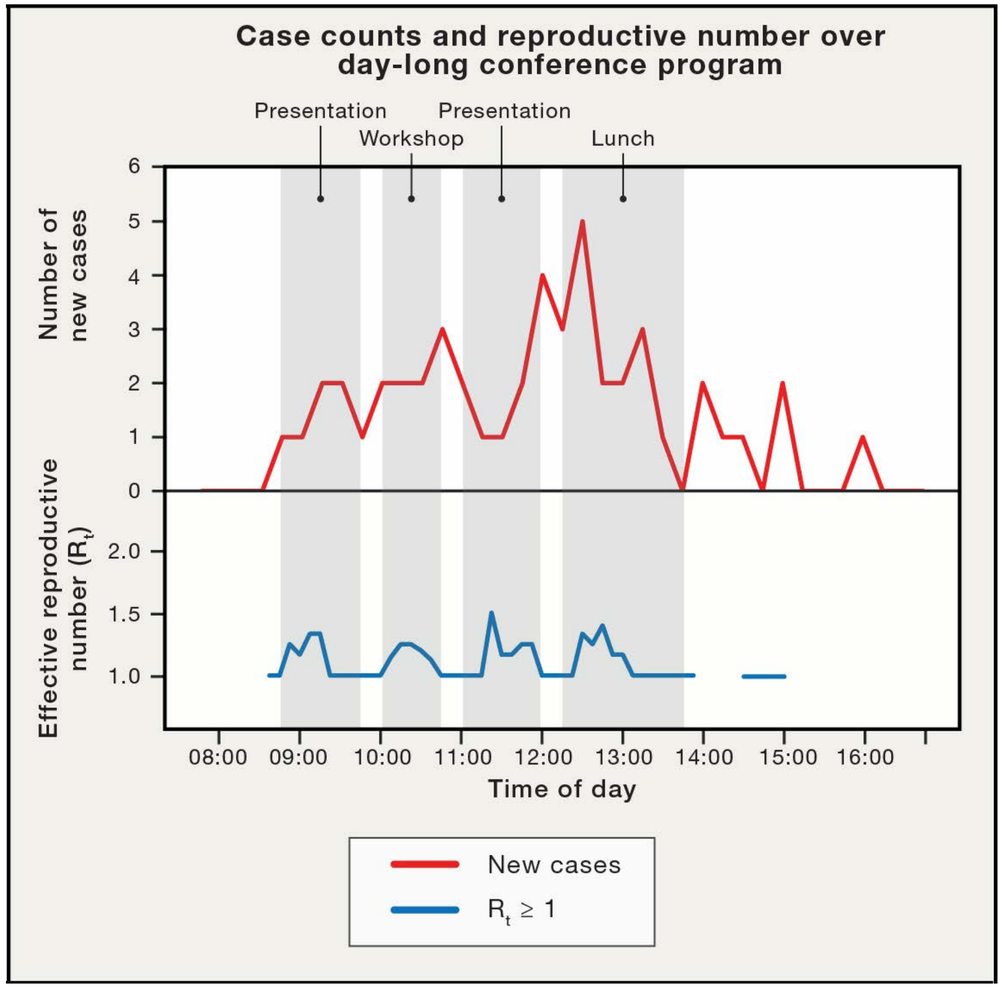
- We set an infectious time of 17 min and a R_0 of ~3.6
- The transmission rate started to decrease approximately 17 min into the simulation
- It halved from its original level just 13 min later

- Students already had expectations about the simulation exercise
- They adopted social distancing behaviors earlier
- Transmission rate halved in only 1 minute

Preventing Outbreaks through Interactive, Experiential Real-Life Simulations. Colubri A et al. *Cell* (2020)

https://github.com/broadinstitute/operation-outbreak-data-models

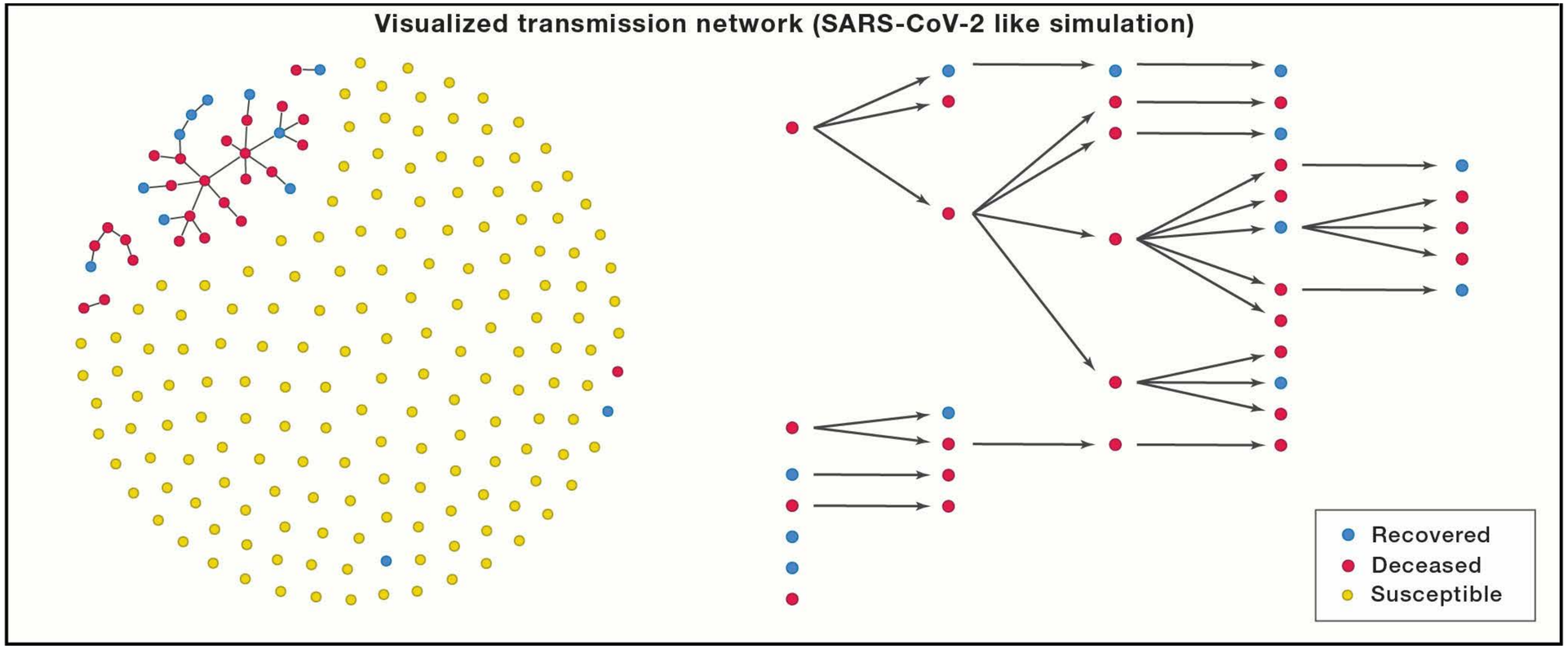
Some results from these simulations



FURC simulation: Only 40% of conference attendees installed the app, leaving susceptible players buffered from each other by non-participants

The effective reproductive number remained below but spiked during activities that required attendees to be in close proximity to each other

Detailed ground truth epidemiological data



Realistic simulated outbreaks provide a unique opportunity to capture not only behavioral changes in response to viral spread but also the “ground truth” of transmission, i.e., documentation of every single event

Role-playing accounts for human behavior

We observed real-life-like behaviors during the simulated outbreaks at SMA:

- Government officials were videoed trying to secure access to vaccine stocks before everyone else and were exposed by the media
- Students took a screenshot of the app in the healthy state, and showed the screenshot to the military to avoid being quarantined

During OO simulations, we observed that players behaved in very realistic ways. Role-playing games allow incorporating social chaos and irrationality in a way mathematical models cannot.

ANDRES COLUBRI TODD BROWN PARDIS C. SABETI SCIENCE 03.13.2019 09:00 AM

When It Comes to Disease, Why Wait for a Pandemic to Respond?

Simulated real-world outbreaks are key to understanding how humans respond to outbreaks—and they provide valuable STEM education to boot.

Ultimately simulations make clear, as in real life, that preparation and cooperation are essential elements for a successful response to outbreaks. And they increase our empathy, allowing us to see first-hand how challenging it might be to be a scientist fighting disease, a health care worker taking care of patients, or a government official planning and executing an effective response to an emergency situation.

Why wait for a pandemic to learn such important lessons?

Operation Outbreak during COVID

CDC Student Programs and Partnerships

Chicago Public Schools

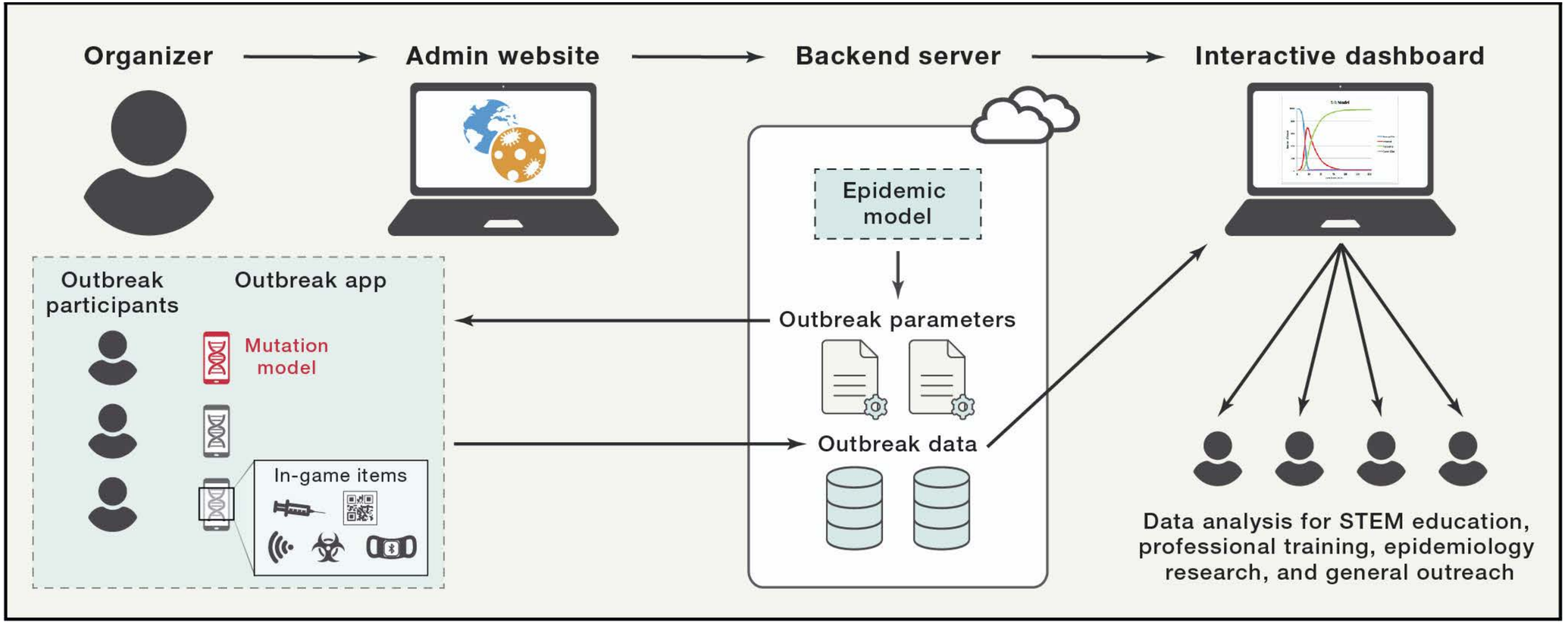
Colorado Mesa University

Florida Gulf Coast University

Needham High School

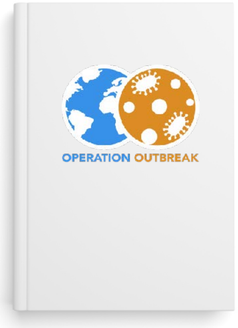
Louisiana Tech University

Agastya Foundation (India)



Operation Outbreak low-tech simulation

Operation Outbreak science textbook



Operation Outbreak Online simulations

What about ORAN?

Meta-modeling with ORAN

$$\frac{dS}{dt} = -\frac{\beta SI}{N}$$

$$\frac{dE}{dt} = \frac{\beta SI}{N} - \sigma E$$

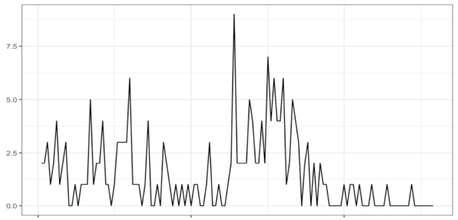
$$\frac{dI}{dt} = \sigma E - \gamma I$$

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

Parameter estimation methods

β
γ
ψ
q

Parameter estimates



OPERATION OUTBREAK

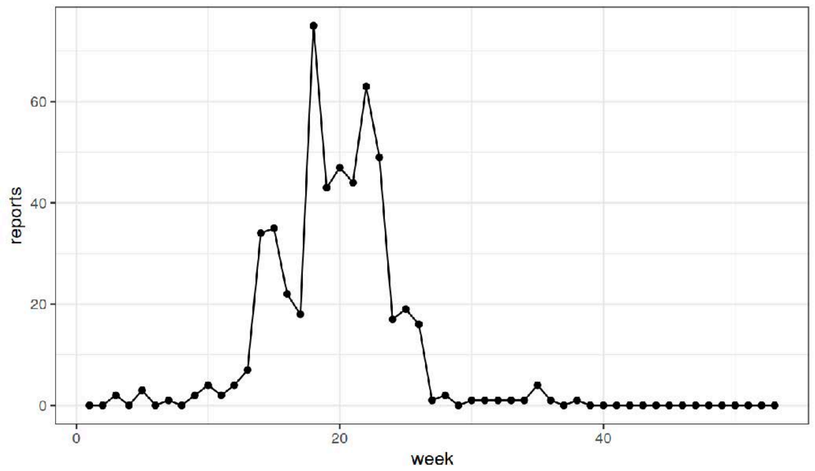
Ground truth epidemiological model

Susceptible β Exposed σ Infectious γ Removed

Epidemiological modeling

Some problems I'm interested in:

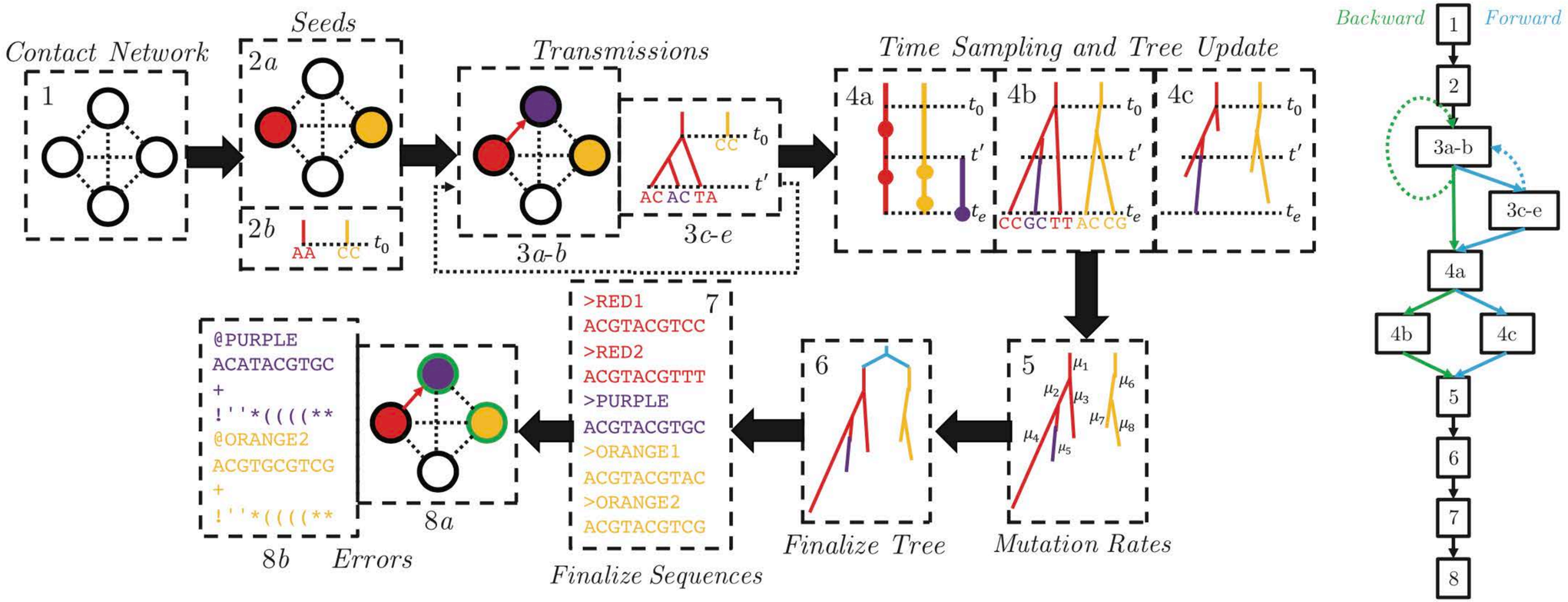
- Can we design OO simulations to validate different modeling approaches?
- How to use OO data (i.e.: contact matrices) to inform epidemiological predictions
- Connecting population-level (compartmental) with individual level (agent-based) models



Simulating pathogen evolution?

- Operation Outbreak could also simulate changes in synthetic pathogen genomes
- This simulated data can help evaluate new methods in genetic epidemiology, because their performance is difficult to evaluate without knowing the ground truth of the outbreak under study
- There are many software tools that do this: **epi-net**, **outbreaker**, **SEEDY**, **FAVITES**

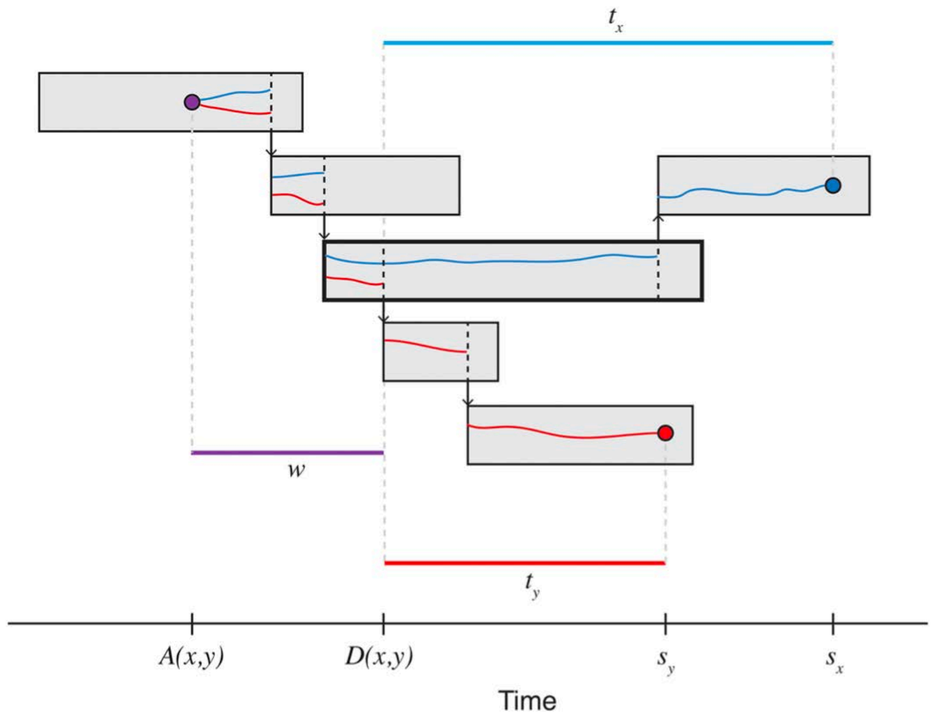
FAVITES: FrAmework for VIral Transmission and Evolution Simulation

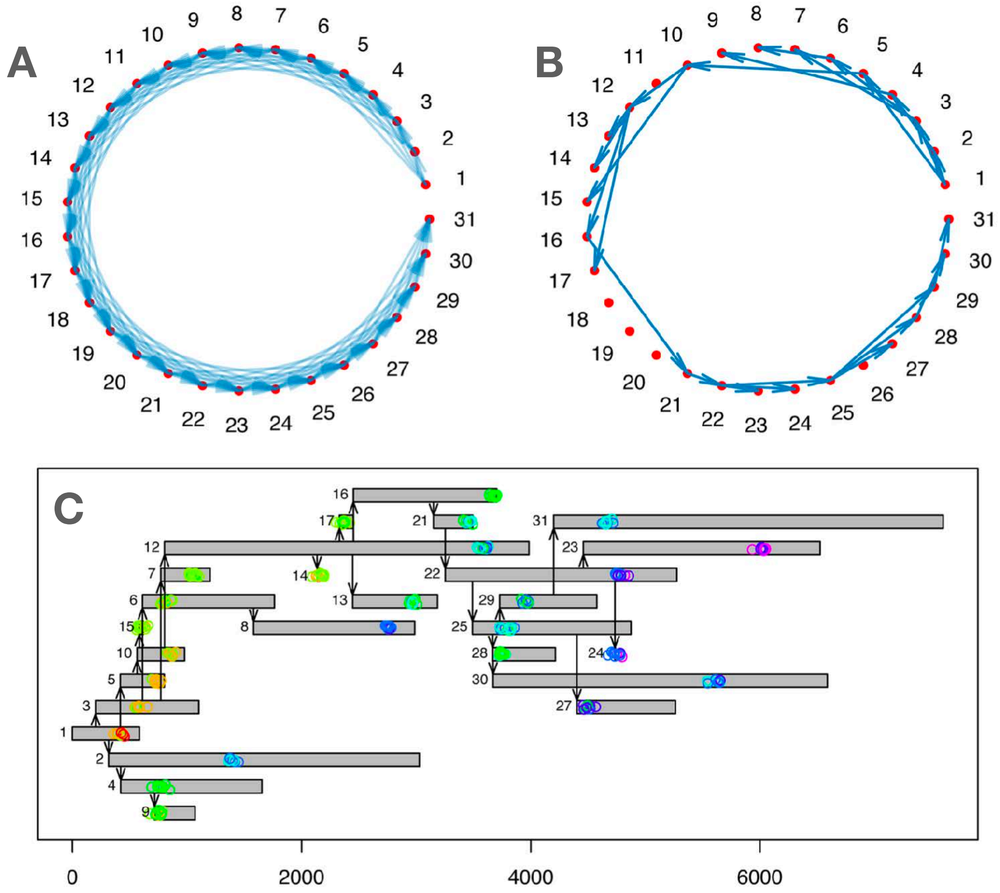


Steps in FAVITES from initial contact network to final phylogenetic tree underlying the transmissions: the epidemic yields a series of transmission events in which the time of the next transmission is chosen, the source and target individuals are chosen, the viral phylogeny in the source node is evolved to the transmission time, viral sequences in the source node are evolved to the transmission time and a viral lineage is chosen to be transmitted from source to destination.

FAVITES: simultaneous simulation of transmission networks, phylogenetic trees and sequences. Moshiri et al. *Bioinformatics* (2018)

A possible algorithm to simulate sequence mutation in OO





Simulated disease transmission and pathogen lineages:

- x (blue) and y (red): two pathogen isolates
- A(x, y): most recent common ancestor
- D(x, y): divergence time
- w: time from coalescence to lineage divergence

Simulated epidemic and genomic sampling in a heterogeneously-mixing population (generated with SEEDY)

A. The contact network of the population
B. Simulated routes of transmission
C. The outbreak and genomic sampling over time.

Conclusions

- Operation Outbreak is a digital epidemiology platform that could support a wide range of applications in infectious disease education and research
- ORAN will complement OO by providing a meta-modeling framework where different models can be used as ground truths to validate model building/fitting approaches
- Operation Outbreak/ORAN will be used to generate epidemiological and phylogenetic models.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USA
AAAS

Todd Brown

Pardis Sabeti

Molly Kemball

Kian Sani

Tomi Siyanbade

Evan Federov

Alex Petty

Jay Doshi

Kaledora Kiernan-Linn

Sol Bloomfield

Kavya Shah

Nathan Hill

Sebastian Agignoae

Rushabh Doshi

Chloe Kazuko Boehm

Thank you!