



Tracking Infectious Disease Spread for Global Pandemic Containment

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Simulation studies play a significant role in supporting pandemic disease scenario prediction and facilitating the understanding of how infectious diseases spread. This is of paramount importance for the anticipation, mitigation, and containment of pandemics. Disease-spread simulation models are often used to understand the effects of changes in citizen behavior or government policies, or to study disease outbreak parameters and mitigation-strategy features. Here, we focus on how to improve future global pandemic containment with the help of advanced artificial intelligence and simulation methods.

Containing Pandemics at the Source

Infectious disease pandemics present serious threats to global health and can potentially impact national security.¹ The Asian-Pacific region is often the epicenter of emerging infectious diseases, having given rise to recent outbreaks of avian flu, Asian flu, and Severe Acute Respiratory Syndrome (SARS). In 2003, SARS affected 29 countries, resulting in 8,096 infections and 774 deaths.² This outbreak demonstrated that increased population density and mobility can play important roles in the spread of emerging infectious diseases and could potentially lead to future pandemics. According to the United Nations Newsletter,³ by 2030 the world's urban population is estimated to reach 8 billion people and the number of city dwellers is expected to grow to 5 billion. People living in urban areas are constantly in close contact, and urban populations experience a vastly different lifestyle than suburban populaces. Mass gatherings of people in confined spaces and interconnected contacts can increase the probability of

spreading infectious diseases.⁴ Even for the same swine flu strain, it has been suggested that the basic reproductive number (a measure of how quickly the disease spreads) in New York City would be greatly different than that found in Mexico City, due to differences in population density, environment, demographics, and behavioral factors.⁵

Taking the 2003 SARS outbreak as an example, we can identify several items of strategic importance. First, the SARS coronavirus at hospital wards critically threatened the lives of healthcare workers and other patients;⁴ and so it's of the utmost necessity to quickly quantify the risk of infectious disease spread within high-risk healthcare facilities to contain the outbreak at the earliest stages. Additionally, today's ubiquitous airplane passenger traffic⁶ and other modes of public transportation result in fast disease movement and variable disease transmission rates, all of which must be taken onto account in any analysis. Further, modeling of detailed community interaction dynamics increases a public health organization's ability to contain a potential strain at its origin.⁷ Traditional influenza simulations typically focus on large-scale populations with a generalized and homogeneous individual contact structure. They often overlook crucial regional variations when constructing community structures and thus are inadequate to replicate the true contact dynamics in the high-population and high-density environments common in urban areas. Moreover, large-scale stochastic models tend to be computationally inefficient if detailed agent dynamics are taken into account; and usually those systems don't provide user-friendly and user-adaptable interfaces.

We envision a systematic, quantitative, and easy-to-use approach for tracking infectious

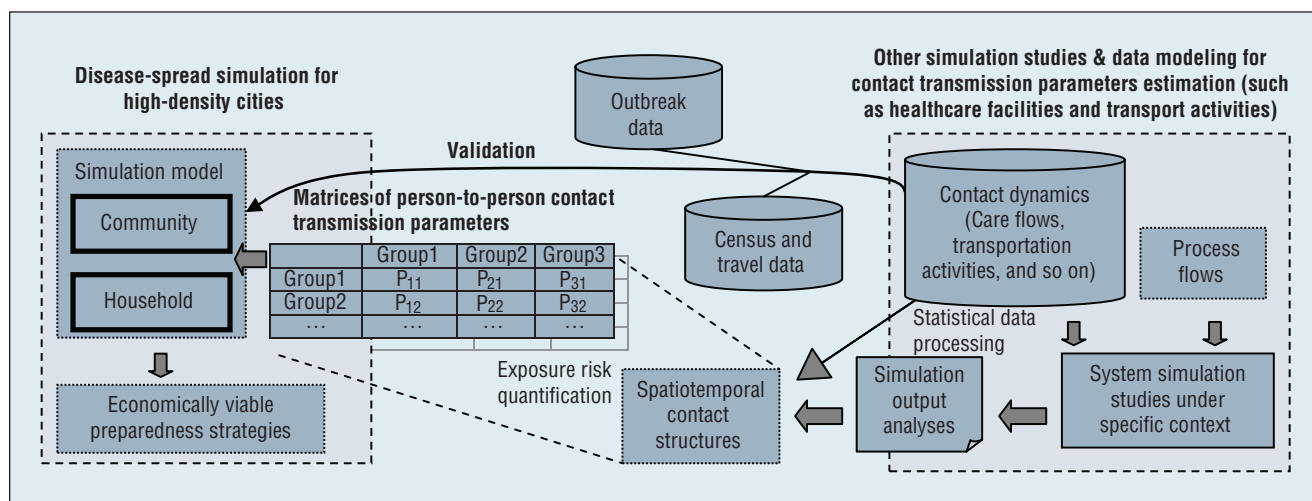


Figure 1. Conceptualizing a disease's spread. Critical social contact simulation model for high-density metropolitan areas. (P = parameters.)

disease spread that can realistically explain critical social contacts and population movements in urban areas. Apart from the health economics implications,⁸ such modeling approaches can enable preemptive detection, identification, and comprehension of pandemic outbreaks, as well as scientific justifications for mitigation strategies, such as social distancing, biosecurity screening, and quarantines.

Considering Critical Social Contacts

Homogeneous mixing models assume that in a given period of time all entities have approximately the same number of contacts, with the same disease transmission probability for each contact. By contrast, a nonhomogeneous mixing model incorporates a variety of contact probabilities, mapping a network of contacts between each member pair in the population. Dionne Aleman and her colleagues⁵ incorporated into their simulation an algorithm to compute each person's probability of becoming infected using his contacts within the population each day. Such an approach may assume varying transmission probabilities, depending on the time and intensity (for example, the spatial

proximity) of each contact. More vulnerable groups, such as children and the elderly, can be identified and modeled by assigning to them higher estimated probabilities of becoming infected than to healthy adults. Superspreading phenomena⁴ by highly contagious and connected individuals can be modeled as well. These kinds of studies also enable the inclusion of indirect disease transmission paths, for instance, through bacteria deposited on a handrail or elevator button. In addition, the flexible modeling paradigm allows for dynamic human behaviors, such as weekly travel or visiting healthcare facilities when infected. Figure 1 conveys the general conceptual framework.

Diseases can be most transmissible when the susceptible group is more vulnerable—for example, when they're sick and housed in hospitals.⁹ Various studies have discussed exposure and infection risk models in local healthcare facilities and special settings such as an isolation ward or general hospital ward.^{10,11} Carline Van den Dool and her colleagues¹² adapted a previously developed model of influenza transmission in a long-term care nursing home to study the effects of the vaccination of healthcare workers in hospital

wards. Moreover, a matrix of healthcare worker-to-patient contact probabilities, numbers of contacts, and times of each contact in hospital settings was proposed.^{12,13} Our team further extended the Susceptible-Exposed-Infected-Removed (SEIR) model (a four-state model used to specify stages of human infection by a contagious disease) from others' work^{13,14} to study how an exposed individual becomes infectious after a latent period during which the individual may experience no symptoms. Preliminary results showed that isolating symptomatic patients can effectively reduce the attack rate (that is, the cumulative infection rate) of patients by more than 10 percent.¹⁵ In the future, categorization of types of patients (for example, by severity of illness) and healthcare professionals (by functions) can help determine the contact structure (in terms of durations and proximities) under hypothetical disease scenarios; additionally, the intensity of contact between healthcare workers and patients can be more accurately modeled through other hospital workflow simulation study platforms.¹⁶

By understanding the spatiotemporal features of contacts between infectious and susceptible persons

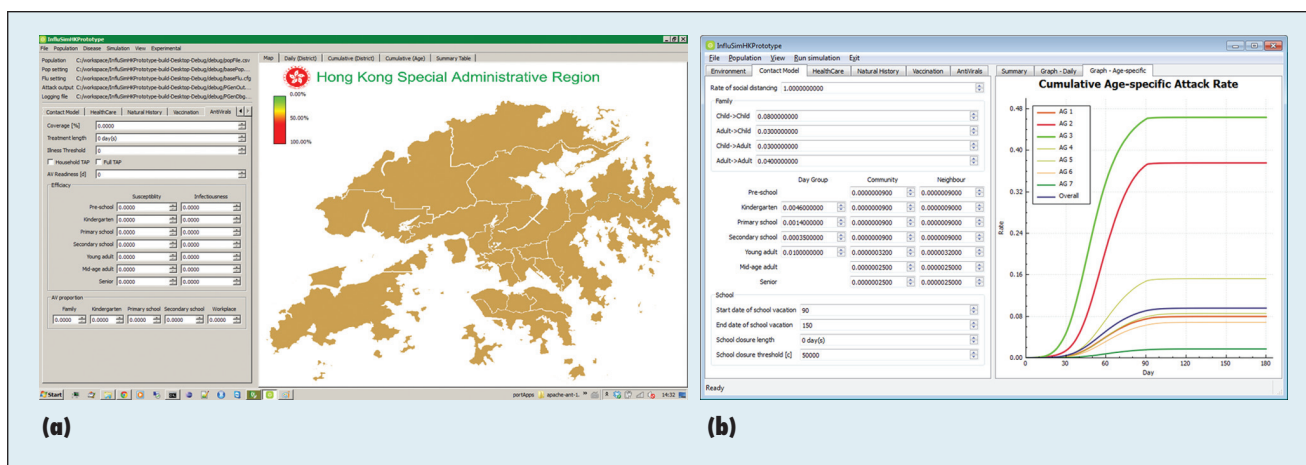


Figure 2. Simulation interface illustrating key output scenarios with respect to Hong Kong's spatial characteristics. (a) Analysis by region. (b) Cumulative age-specific attack rate.

in mass transportation activities, we can quantify the intensity and probability of infection in certain urban settings. Currently, there are some agent-based microscopic models that aim to emulate the movement of passenger flow in frequent public travel activities.^{16–19} Our collaborators studied passenger flow movement via simulation.²⁰ They were able to estimate the probabilities that each individual is in close contact (within 1 meter) or long-distance contact (via an airborne route)²¹ with an infected individual. Thanks to advanced automatic recording and surveillance systems, researchers can capture many passenger movement activities, such as passenger density and ridership flow, station check-in and check-out, and travel patterns. Quantifying domestic travel by age, sex, and the traveler's place of origin, travel duration, and proximity of each contact can improve the modeling of disease spread in major mass-transportation systems within high-density cities.

Efficient Algorithms for Spatiotemporal Simulation

Deterministic models and stochastic models^{7,8,12–14} are commonly used to describe the transmission dynamics of infectious diseases. Deterministic models, formulated by nonlinear

systems of differential equations, are generally applicable to large, homogeneous populations. Disease-spread simulation studies under dynamic parameter assessment, appropriate descriptive granularity of mixing groups, and accommodation of social-behavioral changes are currently feasible, but not yet fully realized. Current global epidemic and mobility models use what is known as meta-population simulation to model the spatial spread of infectious diseases.²² However, tracking every individual's detailed critical behavioral patterns for an entire population can be challenging and requires extensive computation power. Our experience using an agent-based continuous pedestrian model for one metro station with a time step size of 100 ms suggests that such models require significant computing time. The situation can be substantially worsened if we model the detailed travel dynamics and behavioral patterns. Running simulations on parallel computing platforms can be a useful strategy in the face of such challenges, but it isn't feasible in all settings.

It's of great interest to develop algorithms with heterogeneous subset sampling that efficiently draw samples in a domain set with different inclusion probabilities, to simulate

larger-scale populations in greater detail. Meng-Tsung Tsai and his colleagues²³ developed an efficient algorithm for heterogeneous subset sampling, and demonstrated the results in a 23-million agent model of the population of Taiwan. To accelerate stochastic simulation, Ira Longini and his colleagues²⁴ expressed the probability of susceptible persons to become infected as a function of the transmission probabilities from all infectious contacts. We've investigated computationally efficient algorithms with heterogeneous transmission rates by incorporating Bayes' rule.¹⁵ Preliminary results have indicated that computation time can be reduced without significantly sacrificing the accuracy of output results, enabling the simulation algorithm to be run in reasonable time on a standard laptop.

Visual Disease Propagation

Displaying simulation outputs in a user-friendly GUI can facilitate, for purposes of decision making, a visual disease-spread display across a geographical area. Figure 2 presents a preliminary interface design for the simulation package we have developed.¹⁵ Users can investigate how changes in disease parameters and intervention strategies can influence the evolution of an epidemic scenario. The GUI

lets users adjust input parameters and critical interventions in response to a developing outbreak, including demographic composition, transmission probabilities with contact groups, exposure parameters, population sizes, and vaccination coverage levels. The simulation interface also communicates to users several key performance outputs, such as cumulative attack rates by age group. A thematic map shows how the epidemic outbreak is expected to evolve. Such a system lets users assess spatial disease-spread movement and compare dispersion patterns across different demographic dynamics and geographical features. Similar to currently available weather forecast platforms, geographic information system geomapping or mesh grids that provide sufficient accuracy on results displays can be further integrated into visual disease propagation displays.

Despite the many independent surveillance system implementations that have been deployed across different disciplines, such as ESSENCE,²⁵ Google Flu Trends,²⁶ and Global Microbial Identifier (see www.globalmicrobialidentifier.org), our ability to accurately detect infectious disease outbreaks and pandemics is still in its nascent stages. Current surveillance systems lack the means to integrate disparate data sources, although recently proposed methods for multivariate surveillance hold promise for deployment in future systems, and are yet to unify with other surveillance systems to provide accurate prediction for infectious disease outbreaks and spreading trends. Computational epidemiology approaches such as disease detection surveillance, simulation studies, and

microbiological informatics²⁷ can play complementary roles to enable more comprehensive outbreak detection, and are promising in terms of tracking the spread of infectious disease at its origins. Exploring interoperability among different methods for disease detection can justify optimal data-sharing for effective containment of infectious disease spread. The development of robust future approaches involves intimate international scientific collaboration and understanding among statisticians, simulation modelers, epidemiologists, microbiologists, practitioners, and public health policymakers. ■

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