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Chung-Yuan Huang, Yu-Shiuan Tsai and Tzai-Hung Wen

SIMULATION 2010 86: 351 originally published online 11 January 2010

DOI: 10.1177/0037549709340733

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A Network-based Simulation Architecture for Studying Epidemic Dynamics

Chung-Yuan Huang

Department of Computer Science and Information Engineering
and Research Center for Emerging Viral Infections,
Chang Gung University,
259 Wen Hwa 1st Road,
Taoyuan 333, Taiwan

Yu-Shiuan Tsai

Department of Computer Science,
National Chiao Tung University,
1001 Ta Hsueh Road,
Hsinchu 300, Taiwan

Tzai-Hung Wen

Graduate Institute of Epidemiology,
College of Public Health,
National Taiwan University,
17 Xu-Zhou Road,
Taipei 10020, Taiwan
wenthung@gmail.com

Epidemiology instructors are collaborating with computer scientists to construct network-based simulations to recreate infectious disease transmission dynamics and to examine intervention strategy efficacies. Here we propose an architecture based on demographic and geographic properties to support the learning efforts of undergraduate students and novice researchers, and describe our simulations of HIV, SARS, and influenza transmission dynamics in Taiwan. Our findings are offered to support the construction of new network-based epidemic simulations.

Keywords: network-based simulations, epidemic transmission dynamics, SARS, HIV, seasonal influenza

1. Introduction

Computer simulations are now widely used in domains such as sociology [1–4], economics [5], bioinformatics [6, 7], ecology [8], and epidemiology [9]. Examples of specific applications include cellular automata constructed by transportation researchers to evaluate traffic

control strategies [10, 11] and network-based simulations developed by economists to observe cash flow and wealth distribution [12]. Epidemiology instructors are collaborating with computer scientists to analyze the transmission dynamics of infectious diseases, to determine the efficacies of intervention strategies, and to train novice researchers. Until recently, epidemiologists have used questionnaires and field investigation techniques to study epidemic outbreaks: procedures considered deficient for gaining macro views of epidemic dynamics or assessing intervention strategies. Other problems associated with these tools include the inability to capture movement and interaction patterns among millions of individuals with wide ranges of age, profession, education, and disease resistance [13]. As observed in April 2009, epidemic out-

SIMULATION, Vol. 86, Issue 5-6, May-June 2010 351–368
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DOI: 10.1177/0037549709340733
Figures 2, 3, 8, 12, 13 appear in color online:
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breaks can develop randomly and unexpectedly according to such factors as breadth of initial occurrences, number of randomly imported cases, responses of infected individual, the characteristics of contacts with other susceptible individuals, and intervention strategies executed by health authorities.

Network-based simulations are proving successful for exploring epidemic dynamics and assessing intervention strategies among large and varied populations [14–21]. By approaching computational epidemiology from a social network perspective, static domain information such as age, gender, profession, educational level, and marital status can be represented as node attributes. However, dynamic domain information regarding individual factors such as movement and interaction patterns requires support in the form of demographic and geographic data in addition to well-constructed and situation-specific assumptions.

We have used computational modeling and simulation tools to investigate the transmission dynamics of HIV, SARS, and influenza in Taiwan [15, 18–20, 22]. In this paper we (a) propose an architecture based on demographic and geographic properties to teach network-based simulations to undergraduate students and novice researchers, and (b) describe our experiences simulating HIV, SARS, and influenza transmission dynamics in Taiwan, and use our results to illustrate challenges to building network-based epidemic simulations.

2. Epidemic Simulation Benefits

The use of computer simulations as a pedagogical tool is now common in technology training and the teaching of science concepts [22–24]. Epidemiologists are using computer simulations to support education and training efforts based on constructivist learning principles. In addition to mitigating learner obsession with the minutiae of complex procedures described in epidemiology textbooks [25], simulations provide multiple opportunities for ‘learning by doing’ [26]. According to constructivist principles, learners make use of prior knowledge when forming new schema via discovery learning [27]. Confronted with new stimuli, learners apply their knowledge bases to accommodate new information and to alter their existing schema [28]. Applied to epidemic simulations, students will have more and higher-quality opportunities for discovering primary and secondary epidemic issues while gaining hands-on experience dealing with real-world intervention strategies.

Simulations have two characteristics that make them compatible with problem-based learning theory [29].

1. *Engagement.* Students frequently request epidemic simulations to help them gain a sense of real-world epidemiology problems. Simulations also support the introduction of related concepts to the learning

process. There is no ‘perfect’ simulation, but as long as scenario limitations are taken into account they can produce meaningful learning experiences [30].

2. *Interaction flexibility.* When used with interaction and feedback techniques, epidemic simulations help illustrate how infectious diseases are spread under different conditions and various circumstances [30]. The complexity of epidemiology problems means that single ‘correct’ answers are rare, meaning that learners must continuously manipulate parameters. With sufficient practice, students or inexperienced researchers eventually learn how to transfer their new knowledge to real-world infectious disease scenarios.

There are at least three benefits from using simulations to study the spread of epidemic diseases.

1. *Operational.* Epidemiology problems often require examinations of the effects of intervention strategies in specific environments, but real-world experiments are impractical. Using network-based simulations, epidemiologists can examine the influences of different public health policies in different regions, and execute ‘what-if’ experiments to study the emerging behaviors of infections when irrelevant health policies are temporarily removed. For students, simulations can be optimized for learning and training purposes [31].
2. *Observational.* Users can adjust the scales and speed of epidemic simulations for observation purposes. Speeding up simulated processes is considered especially useful for studying the diffusion of diseases such as HIV that have long incubation periods [20]. This allows novice researchers to practice professional skills without having to invest large amounts of resources or becoming involved in high-risk situations. In addition, post-simulation reports allow teachers to determine which concepts their students have mastered [32–34].
3. *Construction.* Epidemic simulations can be used to create and explore various environments. Using intervention strategy assessments as an example, learners can predict developments resulting from different intervention strategy and/or policy combinations, and classroom instructors can exert relatively precise control over knowledge construction and accumulation [32].

3. Network-based Simulations

Compared with agent-based simulations, network-based simulations have a stronger focus on relationships between individuals. In social networks, nodes represent individuals and links their various relationship types. For

instance, in HIV simulations links represent sexual relationships and in SARS simulations they represent close physical proximity. Results from mathematical analyses and experimental simulations indicate that the topological features of social networks exert considerable influence on the transmission dynamics and critical thresholds of infectious diseases, thus supporting analyses of subtle details that non-network-based simulations are incapable of performing [14, 18–20, 35–37]. Furthermore, the need to identify efficient and specifically targeted intervention strategies requires precise representations of demographic and geographic properties such as home quarantines and hospital visitation bans.

Network-based computer simulations imitate interaction and contact patterns between individuals; parallel computing technology is employed to track the movement of heterogeneous individuals. In geographic information systems, regular networks are used to exhibit distance relationships between individuals, for example, von Neumann and Moore neighborhood concepts in two-dimensional regular networks respectively consider a single node's four or eight adjacent nodes as neighbors. The use of regular networks allows for easy representation and measurement of abstract geographic space and distance concepts. In contrast, random networks support features of casual interactions and contacts among mobile individuals, in addition to the low degree of separation commonly observed in social networks.

Network-based simulations have been developed to capture the properties of randomness and geographic distance. One small-world approach to building social networks is the Cellular Automata with Social Mirror Identity Model (CASIMM) (Figure 1) [18, 19]. The social mirror identity concept (Figure 2) allows for simulations of individuals who have regular contact locally and intermittent contact with others over long distances: representative of daily visits to fixed locations and long-distance travel. For the purposes of validation, local and long-distance interactions within a model must correspond to statistical topology features such as a high degree of clustering, low degree of separation, and power-law connectivity distributions.

Different epidemiology issues require different network topology structures for building simulation models based on specific interaction and contact types. For example, HIV diffusion can occur via heterosexual contact, homosexual contact, and illegal drug use, but their network topologies are very different. Heterosexual network models must be scale-free to reflect the statistical power-law distribution of sex partners, but bipartite networks are more likely to accurately reflect the sharing of syringes by injecting drug users (IDUs). Data granularity and detail also affect the topologies of social networks: if a disease control agency can trace all IDU activities, it is possible to build a relatively precise contact network, but if knowledge is limited to specific locations where IDUs congregate, simulations will only reflect more general interac-

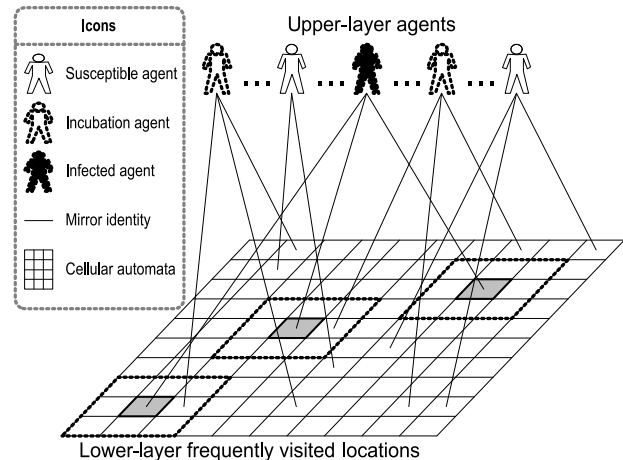


Figure 1. Cellular Automata and Social Mirror Identity Model (CASIMM)

tions and contact pattern assumptions. This explains why demographic and geographic data on individual interactions and contacts are significant challenges for novice researchers learning how to construct network-based epidemic simulations.

4. Network-based Epidemic Simulation Architecture

Two primary issues associated with network-based simulations must be considered when studying epidemic dynamics: choosing an appropriate network model and integrating specific epidemiology domain knowledge and properties. Table 1 shows the individual characteristics most commonly used in network-based epidemic simulations. Several network model types can be adopted, including (a) daily contact networks that utilize individual activity records [14, 21]; (b) bipartite networks composed of individuals and most frequently visited places such as homes, train stations, school buses, workplaces, and restaurants [37]; or (c) CASIMM, which depicts long-distance movement and daily visits to fixed locations [15, 18, 19, 22]. Many epidemiology students struggle with domain knowledge and network construction details such as identifying interaction and contact patterns, choosing/adopting existing network models, and developing/validating new network models.

The four properties considered most important for building epidemiological networks are as follows.

1. *Time scale.* In simulations of HIV diffusion via heterosexual intercourse, sexual behavior frequency distributions over one month or one year will exhibit power-law features [16], but this is not true when the time scale is shortened to one day or one

Table 1. Common individual characteristics used in network-based epidemic simulations

Attribute	Description
<i>ID</i>	Unique serial number identifying each individual.
<i>Mobility</i>	Denotes individual activity. Default value is 'free', i.e. no restrictions on interacting with neighboring individuals. The <i>Mobility</i> status of individuals placed in home quarantine or hospital isolation changes to <i>Quarantined</i> or <i>Isolated</i> , meaning they are restricted to homes, hospitals, or dormitories, and all of their activities are temporarily suspended.
<i>Age</i>	Young (1 to 20), prime (21 to 60), or old (61 and above).
<i>Super Spreader</i>	If yes, set to <i>true</i> ; if no, to <i>false</i> .
<i>Permanent Immunity</i>	If yes, set to <i>true</i> ; if no, to <i>false</i> .
<i>Day</i>	Number of patient days at current disease status.
<i>Contact Rate</i>	Rate of contact with other individuals.
<i>Now State</i>	Current epidemiological progress state.
<i>Next State</i>	Epidemiological state at next time step.

week. It is also important to remember that different diseases have different immunization and incubation periods (5 days for SARS versus 6 months to 20 years for HIV).

2. *Geographic scale.* Whereas CASMIM can be applied to simulate SARS outbreaks in modern cities such as Taipei or Singapore, simulating epidemic dynamics across multiple regions requires additional demographic data. One solution is building one CASMIM for each city and measuring transportation flow between paired cities. Since novel forms of influenza tend to be expressed as large-scale epidemics, models for large regions require consideration of cross-border transportation networks. Furthermore, building social networks for modern cities with established mass transportation systems must assume strong and varied mixes of human movement between cities, between cities and suburbs, and between smaller geographic regions.
3. *Data dependency.* Data granularity determines the best method for building network models. Using homosexual HIV diffusion as an example, when data are limited to frequency distributions of sexual contact, models must be restricted to abstract neighborhood and geographic distance concepts [20]. If movement within high-risk contact populations can be traced, models can be used to predict future development.
4. *Extendibility.* Owing to the diversity of epidemiological data, simulations of specific infectious diseases often require modifications to existing network models. CASMIM is suitable for depicting well-mixed interactions and contact locations for randomly distributed individuals, but it cannot support assumptions of well-mixed locations for sexual contact or needle sharing. Thus, extendibility is a major concern when applying an existing network model to new epidemic simulations.

In response to the range of geographic and demographic restrictions, we propose the use of a four-layer architecture for network-based epidemic simulation construction. The first layer reflects individual-to-individual contact for small-scale social networks. For example, during the 2003 SARS outbreak, health authorities in Taiwan and Singapore attempted to construct contact histories for all infected individuals in order to quarantine anyone coming into contact with a carrier. The second layer consists of passive connections between individuals and locations. For example, saunas and bars frequented by homosexuals are activity locations bridging susceptible individuals with HIV carriers. Among IDUs, infection locations include syringes and chemicals used for drug dilution. To construct IDU social networks, epidemiologists must determine how many times a user shares a syringe with other users during a week/month, and how many users share the same diluting agent in a single session.

The third layer uses abstract geographic properties to reflect individual neighborhood concepts. In the absence of real interaction or contact data, epidemiologists must build well-mixed modern societies based on abstract distances. In previous studies [18, 19] we described a CASMIM consisting of two-dimensional cellular automata as an underlying social network for retaining an individual's geographic mobility. The social mirror identity concept preserves the properties of individuals who interact with their neighbors within two-dimensional geographic spaces, and reflects such activities as long-distance movement and daily visits to fixed locations. The fourth layer often requires significant support in the form of demographic or geographic data. For example, Ferguson's Southeast Asian influenza simulation [17] uses statistical data for population density, household size, age distribution, school and workplace size, and individual travel information. In contrast, the spread of HIV among homosexuals serves as a negative example: movement, location, and means of sexual contact are less obvious, making it more difficult to build four-layer network-based simulations [20].

In the following sections we share our modeling experiences using three of the four layers to construct network-based epidemic simulations. We applied an event-driven programming concept to build the user interface and input/output functions of epidemic simulations. In addition to providing specific statistical reports and charts containing experimental results, the three simulation types allow learners to use browser windows to observe real-time infection situations in agent societies. We used Borland C++ Builder to compile executable applications, therefore our epidemic simulations can be run with specific dynamic linked library files on Windows. For related literature and information, see <http://groups.google.com/group/canslab>.

5. Layer 3: Abstract Geographic SARS Simulation

We developed the CASMIM small-world epidemic simulation model to study SARS transmission dynamics and to assess the efficacies of various intervention strategy combinations. As a robust and extendable simulation model, CASMIM is suitable for classroom demonstrations of epidemiological issues associated with short-distance contagious diseases.

5.1 Data Collection

Most of the epidemic parameter data required for establishing SARS simulations are available from national health authorities or the World Health Organization (WHO). The parameters include R_0 , $Period_{Incubation}$, $Period_{Infectious}$, $Period_{Recovered}$, and $Period_{Immune}$ (Table 2). Epidemiologists and sociologists can provide values for $Rate_{ForeverImmunity}$, $Rate_{Death}$, and average number of social mirror identities. Novice researchers can experiment with the intervention strategy parameters listed in Table 3. Certain parameters such as $Rate_{Infection}$, $Frequency_{Contact}$ can be derived from

$$R_0 = (\text{average number of mirror identity} \\ \times \text{number of neighbors} \times Frequency_{Contact}) \\ \times Rate_{Infection} \times Period_{Infectious}.$$

5.2 Simulation Model

CASMIM [18, 19] is a daily contact network that conceptualizes individuals as elements and their most frequently visited places (homes, train stations, workplaces, restaurants, etc.) as logically abstracted social mirror identities (Figure 1). CASMIM's social mirror identity concept is used to preserve the properties of elements that

Table 2. SARS epidemic parameters

Attribute	Description
R_0	Basic case reproduction number.
$Period_{Incubation}$	Average number of incubation days.
$Period_{Infectious}$	Average number of infectious days.
$Period_{Recovered}$	Average number of recovered days.
$Period_{Immune}$	Average number of days temporarily immune to the disease.
$Rate_{Super}$	Percentage of super-spreaders in total population.
$Rate_{ForeverImmunity}$	Percentage of permanently immune agents in total population.
$Rate_{Death}$	Average death rate.
$Rate_{Infection}$	Average infection rate.
$Frequency_{Contact}$	Number of contacts between an agent and its neighbors per time step.

interact with their neighbors within two-dimensional geographic spaces, and to reflect activities such as long-distance movement and daily visits to fixed locations (Figure 2).

CASMIM consists of an upper layer for simulating heterogeneous cohorts and a lower layer containing two-dimensional cellular automata representing real-world activity spaces. Social mirror identities connecting the two layers establish CASMIM as a small-world social network. Each upper layer individual is depicted as a single agent, and places that an agent visits on a regular basis are defined as its social mirror identities. In a typical cellular automata setup, lattices represent abstract agents; in the case of CASMIM, each lower layer lattice represents a social mirror identity for one individual. It is possible for multiple social mirror identities to be connected to the same agent, with the number exhibiting a normal distribution. Clusters consisting of a social mirror identity and its von Neumann neighbors can represent family members, coworkers, fellow commuters, healthcare workers, relatives in hospitals, or diners in restaurants, among others. Each upper-layer agent has a set of attributes representing its epidemiological progress and social mobility status; these attributes are accessible to all of the agent's social mirror identities (Table 1). In addition, each social mirror identity has a group of private attributes indicating its current status, locations, and special activity locations (e.g. homes, hospitals, dormitories) (Table 4).

Different epidemic simulations require different time steps. For SARS, we defined one time step as equivalent to one day in the real world. Upper-layer agent statuses change simultaneously with their lower-layer social mirror identity statuses during each time step, thereby reflecting their daily interactions. Agent and social mirror identity attributes vary according to four factors: the attributes of neighboring agents' social mirror identities, a set of interaction rules, simulation and epidemic para-

Table 3. Intervention strategy parameters

Policy	Attribute	Description
<i>WearingMaskInGP</i>	<i>RateParticipation</i>	Policy participation rate.
	<i>RatePrevention</i>	Contagious disease prevention rate.
<i>WearingMaskInHW</i>	<i>RateParticipation</i>	Policy participation rate.
	<i>RatePrevention</i>	Contagious disease prevention rate.
<i>TemperatureMeasuring</i>	<i>RateDetection</i>	Fever detection success rate.
	<i>RateParticipation</i>	Measurement participation rate.
<i>HomeQuarantine</i>	<i>Class</i>	A- and B-class quarantines.
	<i>DayQuarantined</i>	Number of home quarantine days.
	<i>RateParticipation</i>	Policy participation rate.
<i>RestrictedAccessToHospitals</i>	<i>RateParticipation</i>	Policy participation rate.
<i>ReducedPublicContact</i>	<i>RateParticipation</i>	Policy participation rate.

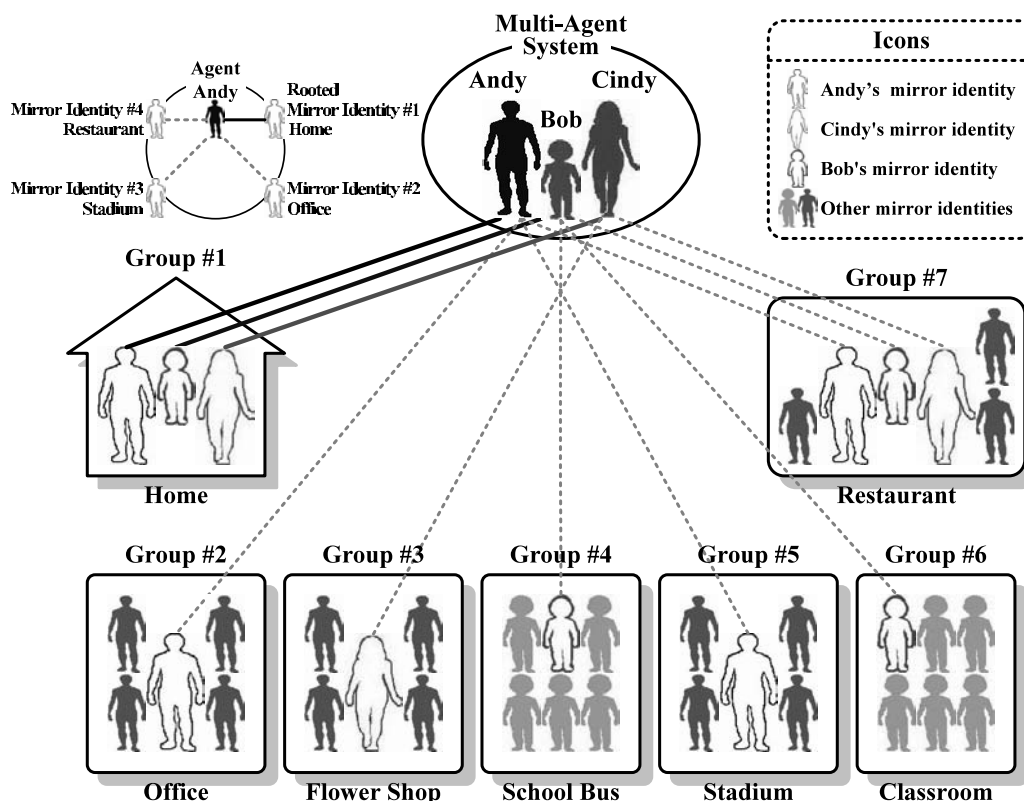


Figure 2. An example of the social mirror identity concept. In the example, Andy spends one hour every morning taking his wife Cindy to her job at a flower shop before driving to his office. Their son Bob takes a school bus to his elementary school. At least once per week, the three of them eat dinner at their favorite restaurant. After dinner, Andy often takes Cindy and Bob home before going with his friends Dick, Eric, and Frank to watch a baseball game. According to our proposed CASMIM, Andy, Bob, Cindy, Dick, Eric, and Frank are upper-layer agents, and the restaurant, stadium, and Andy's home and office are lower-layer mirror identities. Bob's mirror identities are his home, school bus, classroom, and the restaurant. Cindy has only three mirror identities: home, the flower shop, and the restaurant. Andy's car is considered an extension of the family's home node rather than a separate activity node, since Andy rarely uses it to transport anyone other than Cindy or Bob. Bob's school bus is considered a social mirror identity because he uses it five days per week and regularly interacts with many of the children who take the same bus. Andy belongs to one group at home with Cindy and Bob, a second group at his office with his coworkers, a third group (also with Cindy and Bob) with other customers at their favorite restaurant, and a fourth group with his baseball friends. Andy's social mirror identities form a star-shaped topology, with Andy at the center and the mirror identities at the vertices. As shown in Table 4, each individual has one rooted mirror identity. The rooted mirror identity is used to mimic special activity locations, for instance, homes, hospitals, and dormitories.

Table 4. Social mirror identity attributes of individuals

Attribute	Description
<i>Root</i>	Each agent has one mirror identity whose <i>Root</i> = true; for all other mirror identities, <i>Root</i> = false. The rooted mirror identity is used to mimic special activity locations such as homes, hospitals, and dormitories.
<i>Suspend</i>	Default value is false for all mirror identities, denoting an absence of movement restrictions. Except for rooted mirror identities, <i>Suspend</i> = true for all mirror identities of agents in home quarantine or hospital isolation, meaning they cannot interact with adjacent neighbors outside of homes or hospitals until the end of the quarantine or recovery period. When an agent dies, <i>Suspend</i> = true for all of its mirror identities (including rooted), representing the idea that it can no longer visit any other location.
<i>Location</i>	Denotes mirror identity position in a two-dimensional cellular automata. The first number represents the x-axis coordinate, the second number the y-axis coordinate. Each mirror identity is mapped to a single coordinate location; in other words, each location contains a single mirror identity for one agent only.
<i>Neighbor</i>	Coordinate locations of the mirror identities of neighboring agents, based on a Moore neighborhood definition in which each mirror identity has eight neighbors.

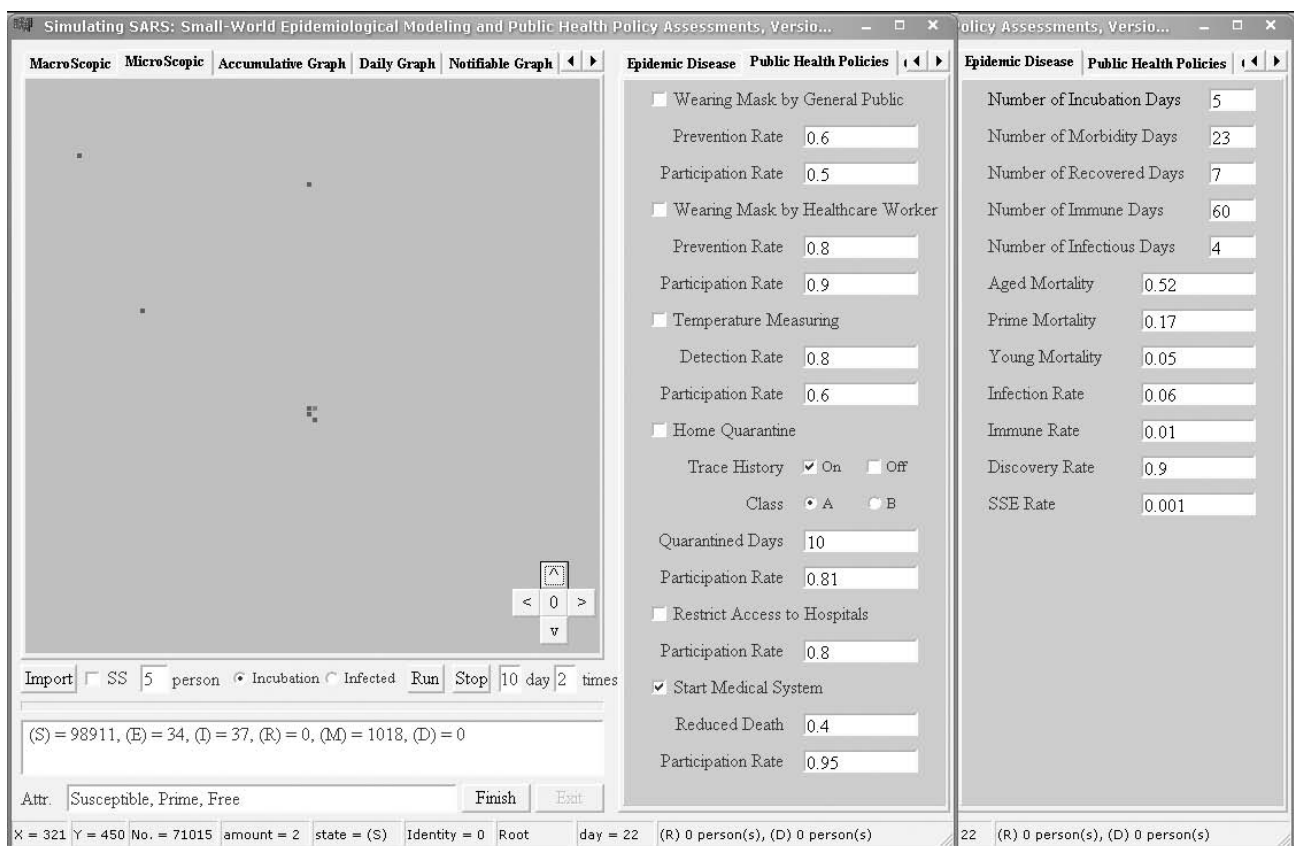


Figure 3. CASMIM simulation console

eters, and intervention strategy parameters. At the beginning of a simulation, learners initialize CASMIM parameters via the user interface (Figure 3, right-hand side), input imported case data, start the simulation, and advance the date according to the SARS outbreak or simulation timeline. In the last step, learners activate individual intervention strategies according to the timeline, and alter

any parameter by activating or disabling it while the simulation is running. Epidemic dynamics and intervention strategy efficacies are immediately affected by parameter modifications.

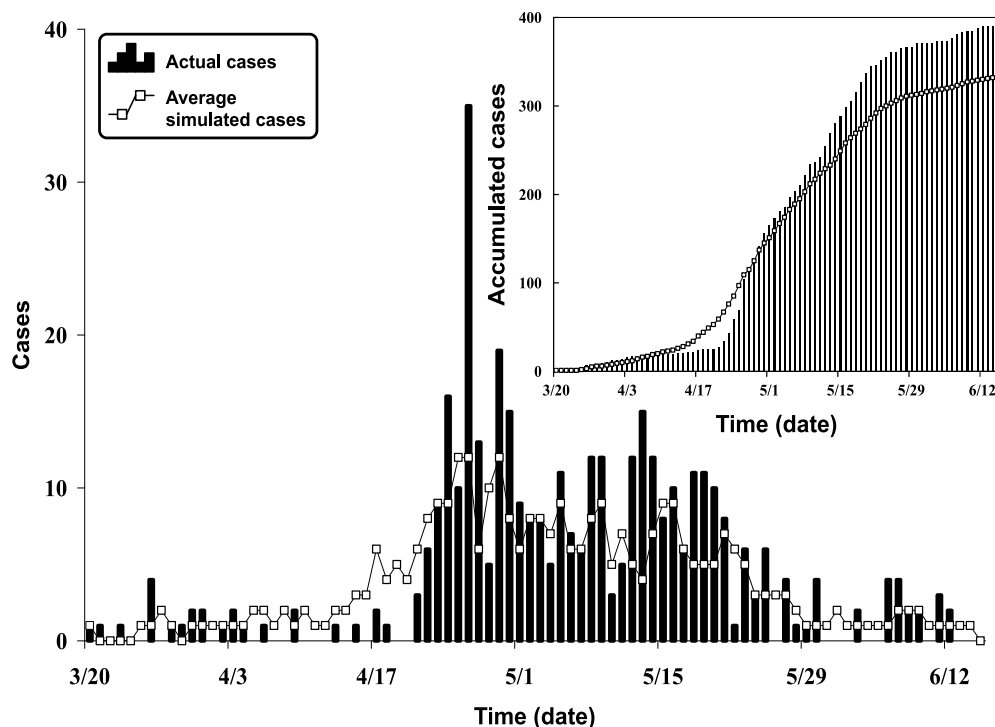


Figure 4. A comparison of actual and simulated epidemic results for the SARS outbreak in Taipei

5.3 Discussion

After initializing CASMIM and setting its parameters using information distributed by national health authorities and the WHO (Tables 1 and 4), learners can simulate SARS transmission dynamics in different cities. Using Taipei as an example, our simulation included several intervention strategies enforced by that city's government, including multiple grades of quarantines and a mask-wearing requirement for all public bus and train passengers. As shown in Figure 4, the simulated curve had a close fit with the actual epidemic curve published by Taiwanese health authorities on September 28, 2003. The higher concentration was likely due to late case discoveries, delays in seeking treatment, illness cover-ups, and the large number of cases imported by travelers returning from Hong Kong.

When faced with a contagious disease outbreak, decision makers must consider various combinations of intervention strategies and decide when to activate them. The compound effects of separate combinations can differ greatly due to the scales, efficacies, and targets of individual strategies. We simulated a strategy suite consisting of the large-scale taking of body temperatures, restrictions on hospital visits, the mandatory wearing of high-efficiency masks by healthcare workers, an advisory for the general public to wear less-efficient masks, and recommendations to reduce public contact. According to the

simulation results presented in Figure 5, a combination of mask wearing by the general public and reduced contact in public places was most successful for suppressing the spread of SARS. Note that enforced mask wearing entails some social and financial costs, but limited public contact does not.

Our simulation results also suggest that a combination of temperature measurement, restricted hospital visitations, and mask-wearing by healthcare workers should only be considered remedial reactions to any contagious disease outbreak, since they do not affect patients who are in the incubation stage or suffering from minor symptoms. In addition, this strategy suite requires substantial amounts of labor and material resources. The combination of home quarantine and reduced contact in public places has high social costs, with results dependent upon how well the isolation guidelines are followed. Numerous instances of intra-family infections were reported during the 2003 SARS outbreak: evidence that certain prevention strategies were ineffective.

To simultaneously assess efficacy and costs, epidemiology instructors must help their students recognize differences in how governments implement intervention strategies, and then encourage discussion of the effects of limited resource allocations. Resources such as vaccines, hospital beds, healthcare workers, and high-efficiency protection masks may be extremely limited or non-existent for an unidentified large-scale epidemic outbreak. Allo-

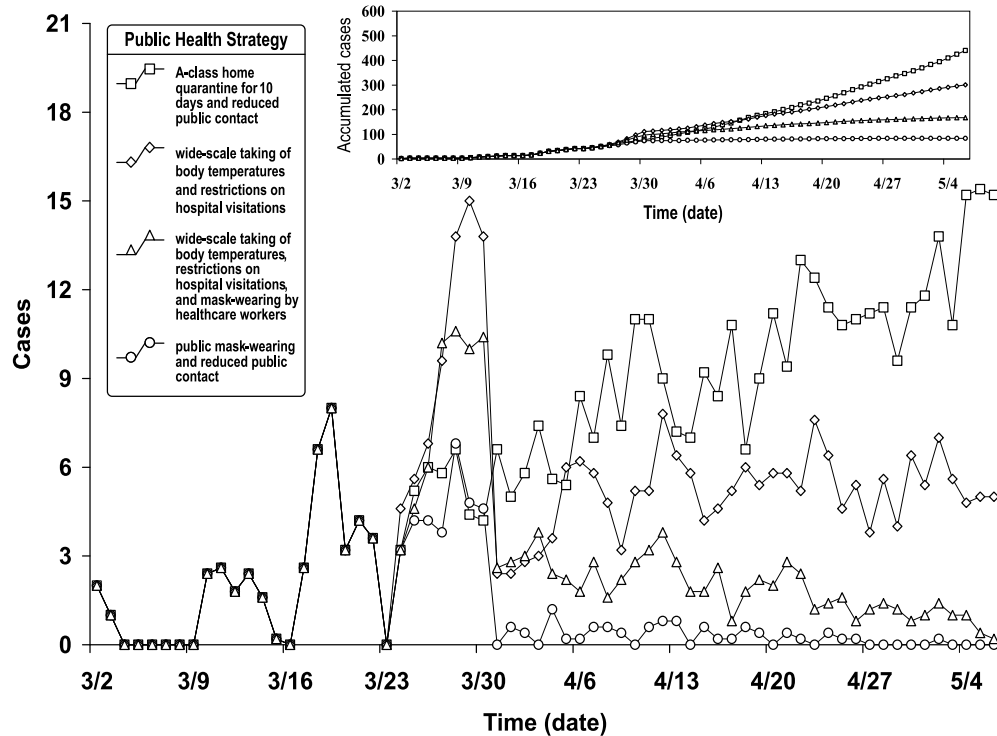


Figure 5. A comparison of various public health policy suites in the third instructional simulation experiment. We used the eight imported cases reported in Singapore to trigger the simulation. Policy suites went into effect on day 24 of our 66-day simulation. Suite 1: A-class home quarantine for 10 days and reduced public contact. Suite 2: wide-scale taking of body temperatures and a restriction on hospital visitations. Suite 3: wide-scale taking of body temperatures, a restriction on hospital visitations, and mask wearing by healthcare workers. Suite 4: public mask wearing and reduced public contact.

cating limited resources should be a central learning objective for students working with large-scale epidemic simulations.

6. Layer 2: Bipartite Network HIV Epidemic Simulation Involving IDUs

According to annual statistics presented by Taiwanese health authorities [38], the number of HIV-1-infected patients increased nationally from 861 in 2003 to 1,519 in 2004 to 3,386 in 2005 (Figure 6). The proportion of IDUs in this population increased from 8.6% in 2003 to 35.8% in 2004 to 71% in 2005 (see [20]). In light of these sharp increases, government agencies initiated several projects aimed at identifying at-risk populations and controlling the rate of new infections. Owing to our success simulating the 2003 SARS outbreak [18, 19], we were asked by the Taiwan Centers for Disease Control (CDC) to collaborate with Professor Yi-Ming A. Chen of the AIDS Prevention and Research Center of National Yang-Ming University to build a network-based epidemic simulation capable of predicting HIV-1 infections among Taiwanese IDUs.

6.1 Data Collection

We used data on HIV-positive Taiwanese gathered between 1984 and 2008. Between November 2004 and December 2006 we collected HIV-1-seropositive blood samples and conducted questionnaire interviews with 518 inmates living in four detention centers and two prisons across Taiwan. Of these, 3% were teenagers, 73% adults, and 24% adults 60 years of age or older (mean age 32.6 ± 7.7 years). A large majority (505, or 97.4%) described themselves as IDUs. The women in our sample were three times more likely than their male counterparts to have had sex partners who were also IDUs (65.8% versus 19.4%). On average, each IDU shared a drug dilution chemical with two or three other IDUs between two and three times per month; 86.9% stated that they had shared heroin diluent, and 98% said they had shared either diluent or syringes. Results from a logistic regression produced 17.2, 34.0, and 46.7 odds ratios for sharing heroin diluent, sharing syringes, or sharing both diluent and syringes, respectively. In summary, the most important HIV-1 infection factors for the IDUs in our sample were heroin dilution sharing, syringe sharing, number of IDUs using the same syringe, and education level.

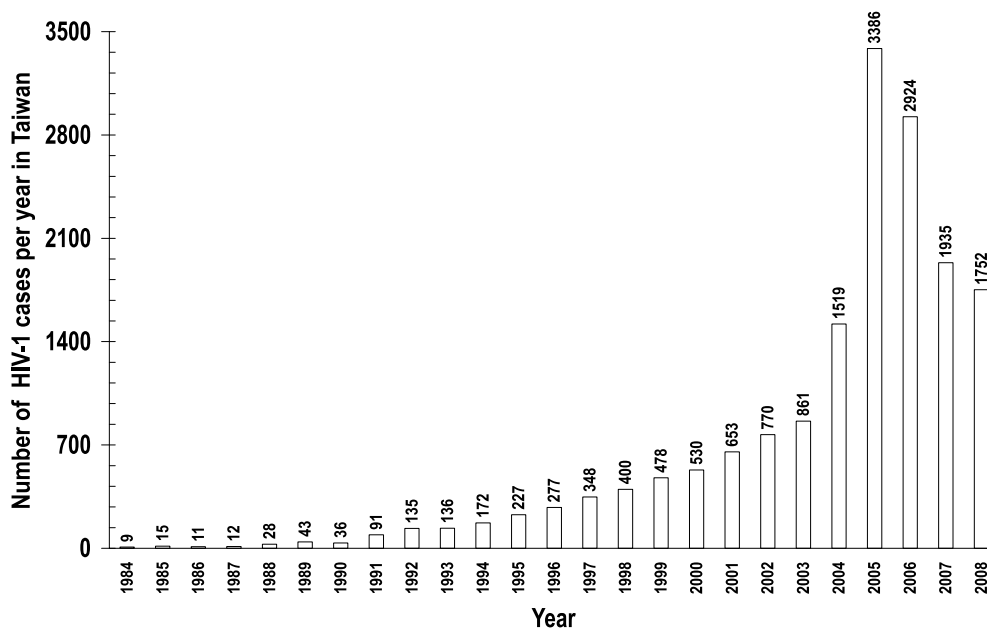


Figure 6. Number of HIV-1 infections in Taiwan from January 1984 to December 2008

6.2 Simulation Model

Since our data were limited to the average number of syringe and diluent-sharing events per month and average number of persons sharing them per occasion, we treated users as abstract neighbors when developing a bipartite network model based on our social mirror identity concept (Figure 7). The model consisted of two layers connected by social mirror identities: an upper layer representing real-world high-risk locations, and a lower layer for simulating IDUs. The ‘P’ individual in Figure 7 visited more high-risk places than other IDUs; ‘L’ marks a frequently visited gathering place.

The time unit used in this simulation was equivalent to one month in the real world. Results and epidemic curves are reported for each year. We used the average number of syringe and diluent-sharing events per month to represent the number of social mirror identities belonging to a lower layer IDU. For the upper layer we used the average number of persons sharing either syringes or a chemical diluent during each occasion to represent the number of IDUs gathered at a high-risk location. Real-world IDU gathering places are located throughout the country and in multiple locations in individual cities, meaning that the spread of HIV among different high-risk locations has no effect on local spreading. In contrast, note that the CASMIM for our SARS simulation incorporated the effect of local spreading, meaning that SARS could still spread to any other location via transmission between local neighbors in the absence of social mirror identities or shortcuts. Since these high-risk locations are not adjacent, the same

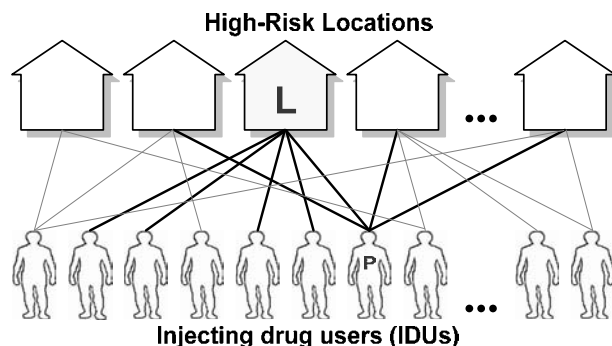


Figure 7. Bipartite relations among injecting drug users (IDUs) and their meeting locations.

CASMIM is inappropriate for simulating HIV transmission among IDUs.

While we were able to obtain data on the statistical distribution of shared syringe and diluent events, we had no data on the statistical distribution of IDUs at each location. According to the most common topological features of social networks, we assumed that this reflects a power-law connectivity distribution. However, we had insufficient empirical data for model validation, especially since the reported number of infected individuals may not have contained concealed cases. This situation shows how difficult it is to build a HIV epidemic simulation without sufficient support in the form of demographic data for building detailed syringe and diluent-sharing rules for IDUs.

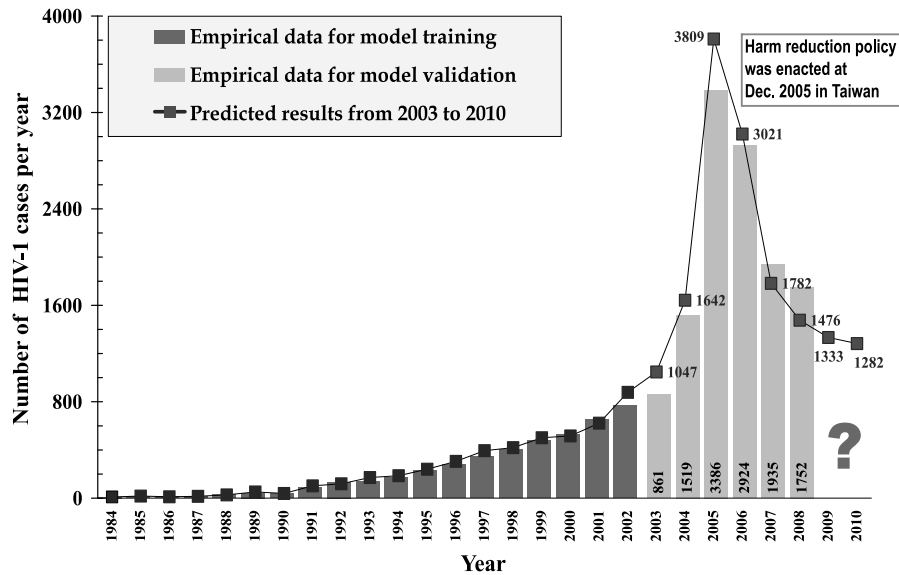


Figure 8. A comparison of actual and predicted HIV epidemic curves from 2003 to 2010 in Taiwan. In this prediction simulation, we averaged 1,000 independent experiments to obtain the mean value of error in the epidemic parameter space, then chose parameters and designated those with minimum mean error as optimal parameters. As shown in the figure, our prediction results correspond to the best among 30 simulations according to the optimal parameters. The parameters did not change over time, that is, predictions were only valid for cases with no additional interventions.

6.3 Discussion

In Figure 8, the dark gray (blue) bar represents 19 years (1984–2002) of HIV data used for model training and fitting, and the light gray (pink) bar represents 6 years (2003–2008) of data used for model testing and validation. For each simulation we activated a harm reduction policy in December 2005 (time step 264) and increased the policy participation rate from 30% to 80% in June 2006 (time step 270). Prediction results are presented as the (red) block curve (2003–2010). Pre-2006 results exceeded actual 2003–2008 HIV epidemic curves (e.g. 1,047 cases predicted for 2003 compared with 861 actual), while post-2007 results were less than the actual number (1,782 versus 1,935).

Taiwanese health authorities initiated a HIV harm reduction policy in December 2005. Despite the low participation rate (30%), it exerted a strong positive effect in terms of controlling the epidemic by reducing the number of new HIV-positive cases from 3,386 to 2,924 by the end of 2006. This represents the first decrease in the number of new HIV cases in Taiwan since 1986. A stronger harm reduction policy was activated in June 2006, resulting in a further decrease in the number of new HIV-positive cases to 1,935 by the end of 2007. Our 2002–2010 simulation results also indicate a decreasing trend, and suggest that an ongoing harm reduction plan would both lower the number of new HIV-positive individuals and reduce the HIV R_0 value from 28 (1984–2006) to 1.1 (2007–2008).

7. Layer 4: Geographic Influenza Simulation

Up to two billion people may be susceptible to the next highly pathogenic influenza virus; the mortality rate could approach 65% (see [39]). According to WHO surveillance reports [40], a novel influenza virus is inevitable, yet it is impossible to predict when and in what form the virus will invade individual countries, or how it will specifically threaten the health of individuals. As this paper was being written, the first reports of a potential swine flu pandemic were being published in media outlets all over the world. Taiwanese health authorities have already announced three major intervention strategies: vaccines, antiviral drugs, and rapid containment operations. As part of this program, in 2006 we joined a two-year project managed by the Taiwan CDC to work with sociologists to develop a multi-region influenza simulation for the entire country. Lacking epidemiological data for prior outbreaks, we simulated the transmission dynamics of seasonal influenza and assessed the efficacies of prevention and intervention strategies to determine the optimal application timing of vaccine and antiviral drug responses.

7.1 Data Collection

We used transportation data to establish a model of daily inter- and intra-regional contact between individuals: specifically, statistics for the average daily movement of railway passengers between counties and cities (Table 5). Demographic data from the 2006 Social Indicators

Table 5. Average numbers of daily passengers using Taiwanese railway transportation by location of residence

No.	Taipei	Taipei	Taoyuan	Hsinchu	Ilan	Miaoli	Taichung	Nantou	Changhua	Yunlin	Chiayi	Tainan	Kaohsiung	Kaohsiung	Penghu	Taitung	Hualien
	City	County	County	County	County	County	County	County	County	County	County	County	City	County	County	County	County
1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	17
1	0	21,996	20,685	1,409	3,587	955	633	146	753	226	148	176	560	157	38	967	7,007
2	16,057	18,344	37,225	1,471	2,365	1,078	703	177	642	191	242	178	582	53	38	1,601	5,183
3	46,249	51,609	12,539	8,411	207	2,335	653	122	684	146	94	122	289	141	63	429	871
4	2,417	2,168	9,308	38	6	7,526	191	22	83	0	0	1	50	2	8	0	112
5	3,122	3,070	344	7	1,917	14	53	12	57	0	0	0	295	12	3	287	1,946
6	1,263	1,005	2,427	4,086	29	416	4,128	98	451	20	30	29	198	30	8	41	163
7	1,507	1,067	749	136	78	4,998	679	7,870	7,420	430	198	204	388	140	53	151	258
8	293	157	78	7	14	39	13,312	0	27,531	2,082	424	89	167	42	10	2	0
9	1,235	727	552	40	23	638	6,993	19,124	207	2,597	3,189	338	724	126	16	104	197
10	342	199	125	2	0	19	372	1,606	2,926	42	10,037	700	652	63	60	0	12
11	236	226	182	5	0	37	247	2,629	1,446	6,091	112	15,897	211	51	13	19	12
12	649	381	245	2	0	50	294	259	687	943	8,560	3,176	10,490	261	110	14	14
13	526	670	297	33	80	225	226	123	520	251	93	2,818	0	58	4,652	1,952	516
14	421	198	239	6	0	13	168	83	248	110	151	8,281	269	119	405	873	307
15	107	76	106	2	0	3	67	15	86	0	0	114	8,070	273	134	1,445	389
16	1,335	1,153	260	0	315	24	156	20	128	5	12	97	20,000	548	1,154	2,464	1,877
17	7,715	4,219	376	84	952	127	114	40	178	0	0	0	462	130	368	1,865	4,007

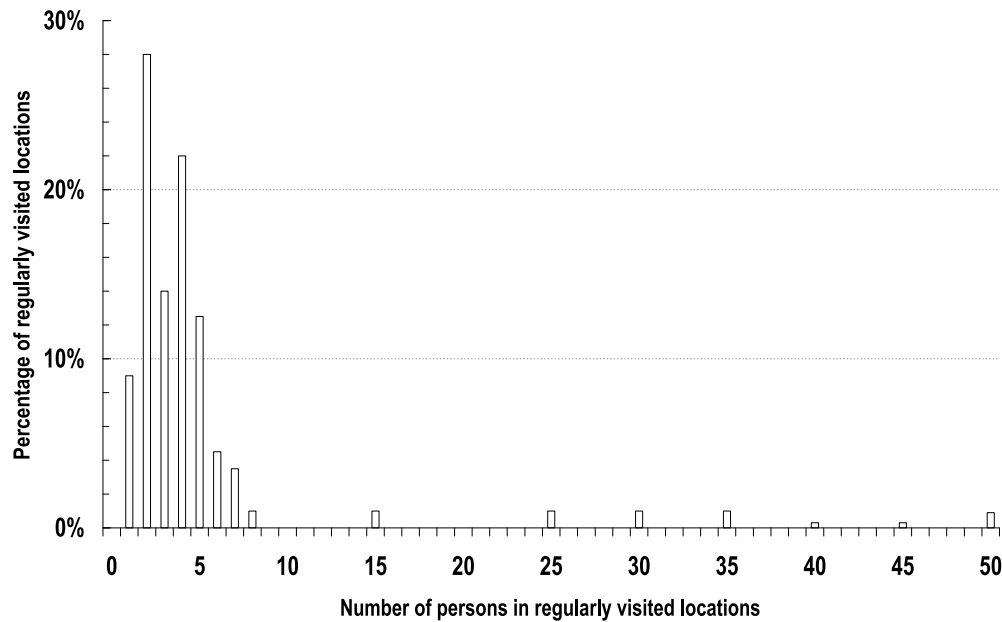


Figure 9. Statistical distribution of numbers of persons in regularly visited locations such as households, workplaces, and classrooms

Report [41] published by the Taiwanese government were used to assign individuals to various locations. These data included statistical distributions of family members per household in each county, numbers of employees in workplaces, and numbers of students in classrooms. We combined data in an effort to achieve an approximate understanding of the overall distribution of the number of persons in each regularly visited activity location. As shown in Figure 9, most activity locations had fewer than 10; exceptions included movie theaters and classrooms, each with 40 or more.

7.2 Simulation Model

Based on our SARS modeling and simulation experience, we knew that CSMIM is suitable for simulating the transmission dynamics of contagious diseases in well-mixed, but not in poorly mixed, modern cities. We therefore assigned a separate CSMIM to each county, with model scale determined by the number of counties included in the overall simulation. Each CSMIM model cell represented one real-world activity location (household, classroom, train station, etc.), and the number of individuals in each cell was assigned according to the statistical distribution of numbers of observed persons in regularly visited locations (Figure 10). Railway transportation data were used to represent inter-county movement, with each instance representing a pair of social mirror identities belonging to the same individual but in different counties. As seen in Figure 10, social mirror identities for the majority of individuals stayed within the same county. Since the incubation period for influenza is only 1–3 days, the

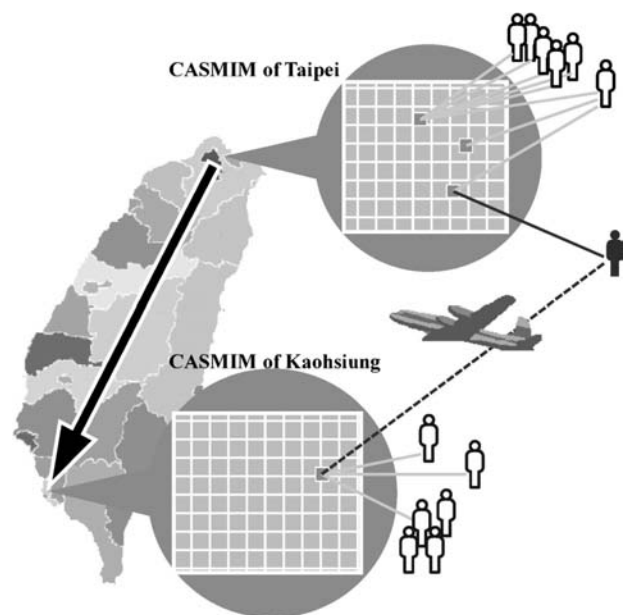


Figure 10. Multiple cellular automata with intra- and inter-city social mirror identities; each mirror identity represents inter-city movement

simulation time unit in this simulation was equivalent to one day in the real world.

The epidemiological progress states for influenza shown in Figure 11 are the same as those described by Longini et al. [42] and used in Stroud et al.'s influ-

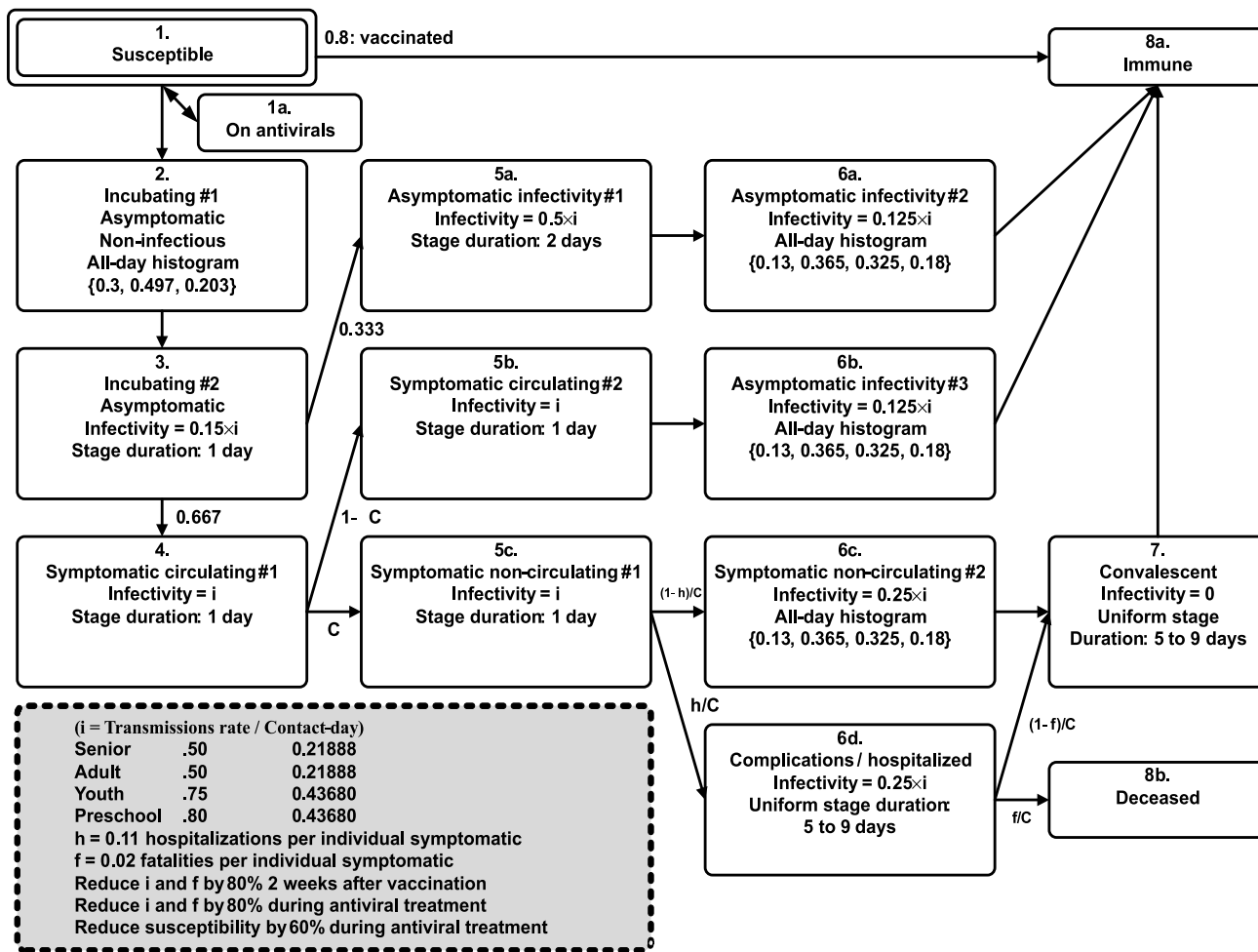


Figure 11. Epidemiological progress states of epidemic influenza disease manifestations for four age categories with no treatment [42, 43]

enza simulation system [43]. Separate epidemiological progress states were implemented for four demographic categories: preschool (younger than 5), youth (between 5 and 21), adult (between 21 and 65), and senior (older than 65). Base infection rate (infectivity level) was established as 0.21888 per contact per day for adults and symptomatic seniors, and 0.43680 per contact per day for symptomatic preschoolers and youths. The rate of asymptomatic infectious individuals was equal to one-half the base infection rate (Figures 5(a) and 11).

One shortcoming of our multi-region influenza simulation model was its lack of network topology properties for an epidemic simulation model consisting of multiple poorly mixed cities. Unlike a well-mixed modern city, modelers cannot assume that interaction and contact networks of individuals distributed among multiple counties have small-world properties. In addition, there is a lack of epidemiological data for recent novel influenza pandemics to use for empirical validation. Some epidemiologists

have constructed simulations of the 1918–1919 influenza pandemic [43], but we believe the network topology structure of modern metropolitan areas is very different from that observed in 1918. Despite these weaknesses, we used our multi-region influenza model to simulate the transmission dynamics of seasonal influenza and to assess the efficacies of a vaccine policy and intervention strategies under different conditions and in different regions.

7.3 Discussion

We used two assessment indicators (prevention effect and cost–efficacy) to replace previously employed epidemic curves to help epidemiologists and public health experts assess the efficacies of intervention strategies. The prevention effect indicator

$$\text{Prevention_effect}(\text{Strategy } A) = \frac{\text{Total infected cases without activating any strategy}}{\text{Total infected cases with } A \text{ activated}} \in [0, \infty] \quad (1)$$

Table 6. Parameter settings for various intervention strategy experiments

Intervention Strategy	Target Group
Inoculate individuals at random.	Entire population.
Locate and inoculate those who have come into contact with infected individuals.	Specific population segments.
Encourage hand washing and mask wearing by the general public during flu season.	All individuals between the ages of 15 and 64.
Quarantine infected individuals until complete recovery. Home quarantine individuals who have come into contact with them for a minimum of eight days.	Specific population segments.
Give anti-virus medicine in advance for prevention purposes.	Entire population.

was used to evaluate specific intervention strategies; its value was set at more than one to produce better effects, since for values less than one the strategy actually supports the spread of a disease. By comparing different policies at this level, public health experts can identify the best intervention strategy. The cost–efficacy indicator

$$\text{Cost_Efficacy(Strategy A)} = \frac{\text{Total infected cases with activating any strategy} - \text{Total infected cases with A activated}}{\text{Total consumed resource costs of A}} \quad (2)$$

was used to evaluate the prevention effect per unit cost; its value was purposefully made positive to produce better effects, since the policy has no preventive effect when the value is zero. Public health experts can use the same benchmark to make decisions regarding the best timing of intervention strategies in response to a novel influenza.

We used our influenza simulation to compare prevention effects and cost-efficacies for five intervention strategies, two regional densities (low and high), and three policy application dates (10/1–10/07, 10/22–10/28, and 11/19–11/25). The five intervention strategies and corresponding objects were (1) giving the vaccine to randomly chosen individuals, (2) tracking and inoculating individuals coming into contact with infected individuals, (3) strongly encouraging hand washing and mask wearing by the general public during the influenza season, (4) enforcing home quarantines for infected individuals until they recover and for individuals who have come into contact with them for a minimum of eight days, and (5) giving anti-virus medicine in advance to all individuals (Table 6). As shown in Figure 12, the two most effective intervention strategies were giving vaccines to randomly chosen individuals and using anti-virus medicines. The combination of encouraging hand washing and mask wearing was the third best. All three policies were more effective when activated as early as possible, with little difference in effect between activating the policies in late October and late November. Our main conclusions derived from the simulation results were (a) the combination of hand washing and mask wearing by the general public during the influenza season is the most cost-effective policy, and (b) using anti-virus medicine in advance is more cost-effective than buying and using a mix of vaccines and anti-virus medicines (Figures 12 and 13).

8. Conclusion

In this paper we have proposed a pre-analysis architecture for network-based epidemic simulations for training students and novice researchers, and have given examples of architecture reductions and extensions in terms of available geographic and demographic data. Epidemiologists can use this information to support such tasks as analyzing spreading situations and outbreak patterns, predicting future transmission dynamics, and assessing the efficacies of intervention strategies for disease prevention and control, vaccine development, and other efforts to fight epidemics. We have also described three sample applications of network-based epidemic simulations.

Based on our experiences teaching epidemiological modeling and simulations, we have identified three challenges for instructors: the choice of a suitable network model, preparation for instruction-based teaching, and evaluating student understanding. Network-based simulations for solving epidemiology issues require more demographic and geographic data support and higher levels of initial domain knowledge. In other words, most epidemiology issues require collaborations among computer scientists, epidemiologists, and policy decision makers.

Developing appropriate prevention and control measures entails making and monitoring the results of multiple rules and decisions made at different points during an epidemic. Conflicts among decision criteria for different strategies are inevitable, and our proposed simulation architecture based on demographic and geographic properties can help decision makers test and refine different intervention strategies at different layers. By analyzing multi-scale interactions, decision makers can prepare themselves for making rapid proactive intervention decisions in response to identified outbreak transmission pathways. Furthermore, our social mirror identity concept can provide additional geospatial insight into epidemiological processes underlying control measures. In the future, spatial orientation and visualization will be required for monitoring disease progress and generating potential control strategies. Our plans include incorporating a geographic information system (GIS) into our architecture and simulations in order to capture spatial variation in disease transmission throughout Taiwan. The GIS will support a visual analysis of the spatial impacts of individual control measures. We believe that combining network-based epi-

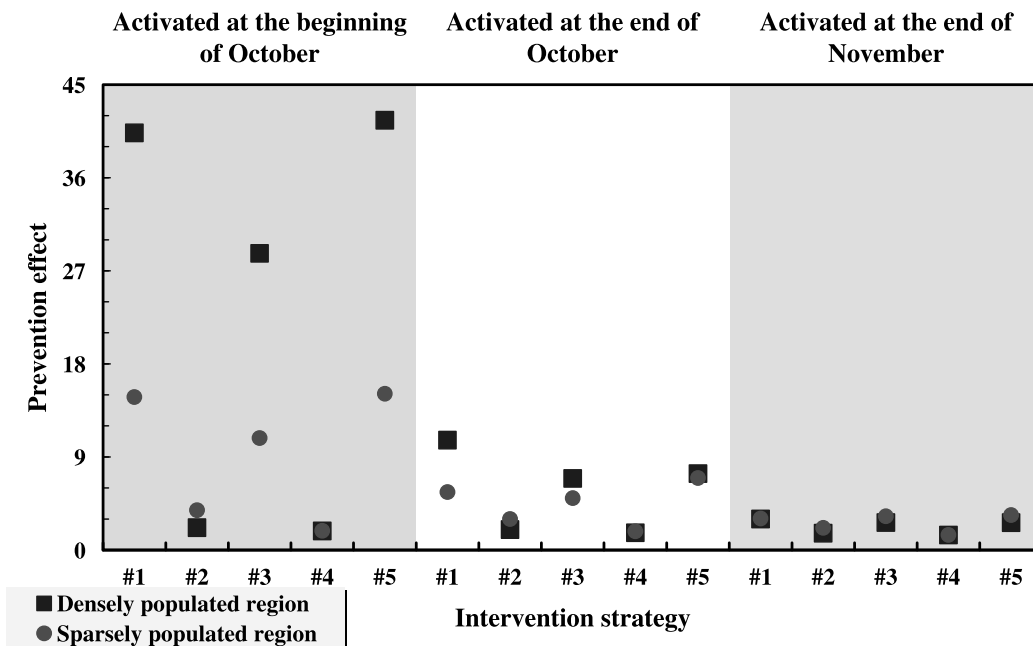


Figure 12. Comparisons of prevention effects among five intervention strategies: 1, inoculate individuals at random; 2, locate and inoculate those who have come into contact with infected individuals; 3, encourage hand washing and mask wearing by the general public during the flu season; 4, quarantine infected individuals until complete recovery, and home quarantine individuals who have come into contact with them for a minimum of eight days; 5, give anti-virus medicine in advance for prevention purposes, activated on three policy activation dates (beginning of October; end of October; end of November) and for different population densities (high and low).

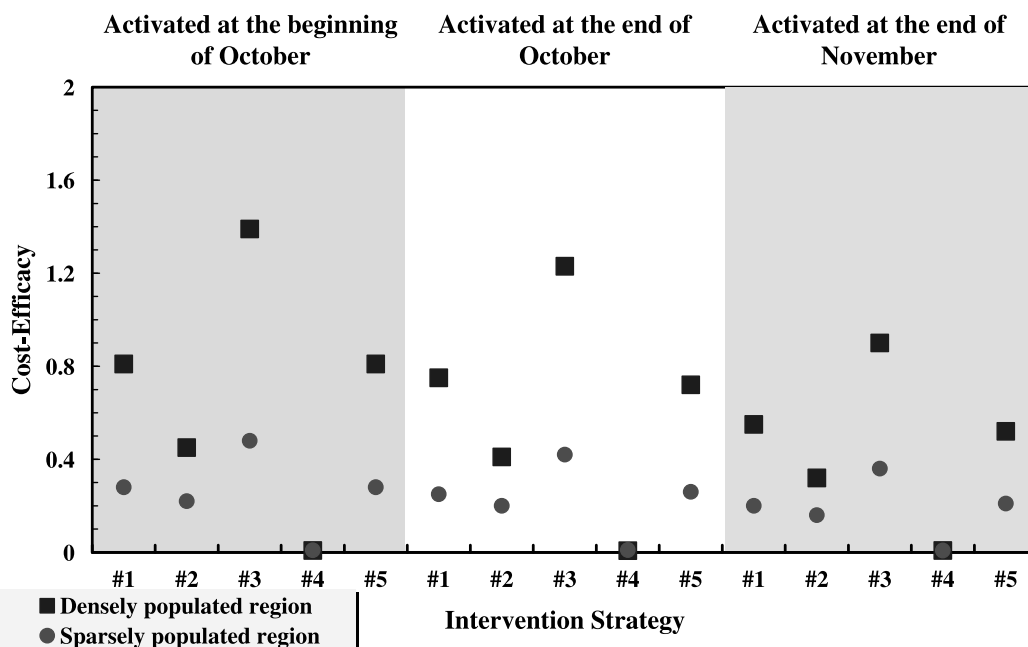


Figure 13. Cost–efficacy comparisons among five intervention strategies as described in Figure 12

demographic simulations, spatial visualization, and geographic information will support the efforts of epidemiologists to clarify spatial and temporal characteristics when analyzing pandemic preparation and control measures.

9. Acknowledgements

This work was supported in part by the Republic of China (ROC) National Science Council (NSC97-2221-E-182-046 and NSC97-2314-B-002-180), Chang Gung University (UERPD270281), and Chang Gung Memorial Hospital (CMRPD260022). Tzai-Hung Wen also acknowledges administrative support from the Infectious Disease Research and Education Center, Department of Health, Executive Yuan, and National Taiwan University.

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Chung-Yuan Huang received his M.S. degree in computer information and science (2000) and his PhD in computer science (2005), both from the National Chiao Tung University, Taiwan. He is currently an Assistant Professor in the Department of Computer Science and Information Engineering and a member

of the Research Center for Emerging Viral Infections at Chang Gung University, Taiwan. His research interests include complex adaptive networks and systems, agent-based modeling and simulation for social science research, and computational epidemiology.

Yu-Shiuan Tsai received his B.S. and M.S. degrees in mathematics from the National Taiwan University, Taiwan, in 2002 and 2005, respectively. He is currently a PhD candidate in the Department of Computer Science, National Chiao Tung University. His current research interests include complex networks and systems, social simulations, and computational epidemiology.

Tzai-Hung Wen (corresponding author) received his PhD degree in 2006 and currently is an Assistant Professor in the Graduate Institute of Epidemiology, National Taiwan University, Taiwan. He is also a faculty member of the Infectious Diseases Research and Education Center at National Taiwan University and Department of Health, Executive Yuan, Taiwan. His research interests cover applications of geographic information systems (GIS) and geospatial modeling in public health-related issues, especially in infectious disease epidemiology and evaluation of control strategies for epidemics.