BioWar: Scalable Agent-based Model of Bioattacks

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***Abstract*—While structured by social and institutional networks, disease outbreaks are modulated by physical, economical, technological, communication, health, and governmental infrastructures. To systematically reason about the nature of outbreaks, the potential outcomes of media, prophylaxis and vaccination campaigns and the relative value of various early warning devices, social context and infrastructure must be considered. Numerical models provide a cost-effective, ethical system for reasoning about such events. BioWar, a scalable city-wide multi-agent network numerical model, is described in this paper. BioWar simulates individuals as agents who are embedded in social, health, and professional networks and tracks the incidence of background and maliciously introduced diseases. In addition to epidemiology, BioWar simulates health care seeking behaviors, absenteeism patterns, and pharmaceutical purchases, information useful for syndromic and behavioral surveillance algorithms.**

***Index Terms*—bioterrorism, multi-agent network, social network, syndromic and behavioral surveillance.**

I. Introduction

THE capability to assess the impacts of large scale biological attacks and the efficacy of response policies is necessary from intelligence and planning perspectives and requires reasoning about social response and disease transmission within a complex social system. The recent case of an atypical pneumonia (SARS) [1] illustrated the importance of and close linkage among social networks [2]-[3], disease transmission, and early detection. Like natural epidemics, biological attacks will also unfold within spatially defined, complex social systems, and the societal response will have profound effects on their outcome.

It is not always clear how best to detect and respond to a disease outbreak, either natural or malicious. The goal of our research is to develop tools to simulate how diseases spread through socially connected groups so that these tools may be used to test the various detection and response options. This paper focuses on bioterrorist attacks, but the model structure has been applied to emergent and familiar diseases as well.

In trying to prepare for attacks, policy makers need to be able to think through the consequences of their decisions in various situations. Role-playing "simulation" physical exercises can provide valuable insights but are limited in number, size, scope, and scenarios due to cost, time, and cognitive constraints [4].

Designed and validated correctly, computer simulations can be more cost-effective, faster, and more comprehensive, allowing enormous numbers of complicated, outside-the-box scenarios to be examined systematically.

Recently, GIS (Geographic Information Systems) based epidemiological models have been developed that take into account the spatial and geographical dimensions [5]-[6], however this work does not consider the social dimension nor the interplay between different dimensions which would affect the complex outcome of the interacting real world systems. There has also been relevant work in RoboCup rescue [7], swarm/ants intelligence [8], and mathematical modeling of multi-agent systems [9]-[10]. While RoboCup rescue is useful for investigating rescue strategies in a simulated earthquake, it is concerned with designing smart algorithms, not with investigating a current human social system as it exists and designing a public policy for it. The swarm/ants intelligence work focuses on the emergence of smart group behaviors out of simple individual routines (e.g. for those of insects such as ants), instead of on knowledge-intensive and context-intensive human social system and the effects of epidemics within it. The mathematical modeling of multi-agent systems is an idealized approach to modeling social systems that is good at describing population dynamics. It concerns itself with deriving equations to describe macro-behaviors from micro-behaviors, often needing to make assumptions such as the use of a generalized Markov model, which are not necessarily sufficient to describe social systems.

BioWar is a single integrated model of the impact of a bioterrorist attack on a city that combines state-of-the-art

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computational models of social networks, communication media, and disease transmission with demographically resolved agent models, urban spatial models, weather models, and a diagnostic error model. Unlike traditional models that look at hypothetical cities, BioWar is configured to represent real cities by incorporating census data, school district boundaries, and other publicly available information. Moreover, rather than just providing information on the number of infections, BioWar models the agents as they go about their lives – both the healthy and the infected. This enables observation of the repercussions of various attacks and containment policies through natural measures such as absenteeism, medical website hits, medical phone calls, insurance claims, over-the-counter pharmacy purchases, and hospital visit rates, among others. BioWar is useful for clients concerned with preparedness training, response analysis, detection algorithms evaluation, stakeholder communication, and public policy analysis. The intended user base of BioWar is policy analysts and developers representing such clients. Versions of BioWar have been made available to several outside groups, including Charles River Analytics, Inc. and the US Army. As it presently stands, BioWar still requires expert users: we are in the final phase of developing a simplified graphical user interface implementation.

II. Limitations of Previous Epidemiological Models

Epidemiologists have used the SIR (Susceptible-Infected-Recovered) framing for modeling the course of epidemics [11]. Such models are typically implemented assuming homogeneously mixing populations, with no medical intervention, no spatial dimension, no social (and network) connections [12], nor symptom-based behavior.

Cellular-automata models for disease spread, such as the Brookings' individual-based computational model of smallpox epidemics [13], improve upon the differential model of SIR, allowing spatial operation and discontinuities. The geometry of cellular automata, however, does not match the spatial reality of the real world, oversimplifying disease propagation processes.

System dynamics models such as Epi-Engine of CiMeRC (National Bioterrorism Civilian Medical Response Center) abstract away the underlying social interactions with a system of mathematical equations [14]. While system dynamics models capture the general trend of epidemics and feedback loops, they are problematic for the subtleties of micro- and meso-behaviors, and they largely ignore the symbolic aspects of a population such as knowledge about school districts, recreational preferences, the calendar of events and holidays, and traffic regulations, among others.

A discrete event simulation model of antibiotic distribution was used to examine post-exposure prophylaxis [15]. Though providing useful insights, it did not model the social interactions and physical dimensions of disease spread and response.

Purdue University's Measured Response simulation model is based on Synthetic Environment for Analysis and Simulation (SEAS), a DNA-like agent model for a synthetic economy [16]. The model represents agent inputs/sensors as binary "genes" and agent outputs/actions/decision factors as binary "genes" (e.g. financial security and liberty genes). The model has a routine that determines the mapping between its input and output attributes/genes, and updates the state of its genes. Measured Response model has been used for annual training exercises of the same name with local, state, and federal officials as participants, and has a good interactive interface. The model however often uses abstract/high-level entities and behaviors as genes, ignoring the major raison d'être of the multi-agent simulations: emergence of high-level behaviors and entities from low-level primitives. This is relevant to the ability to examine micro- and emergent meso- and macro-behaviors of agents crucial to the effective response against a bioterrorism attack. Non-binary and non-Markovian input and output values are not modeled. The complexity and nuance of social interactions, including the co-evolution of cognition and structure – a factor in disease spread – are overlooked. Measured Response applies population-based mathematical models as determinants on agents, instead of allowing for emergence. It models individual attack diseases alone without concurrently simulating normally occurring diseases, and does not properly model disease progression, disease confounding, symptoms, diagnosis, treatment, or individual response to symptoms and diseases. The Measured Response model and its model assumptions and variables have not been validated; in particular, its disease model has not been validated against empirical data of past outbreaks. Its hypothetical simulations of a stylized city are inadequate in fidelity, partially because it does not have proper spatiotemporal coordinates, spatial regions, and spatial operations such as proximity and adjacency. To meet the requirement to simulate at varying scales (e.g. local, state, and national), Measured Response imposes these levels onto its agent model by using small numbers of agents to represent large populations but does not provide adequate scientific justifications as to what level of abstraction and how much aggregation and layering are feasible without reducing its agents into simple homogeneous sample populations, forgoing the benefits of agent-based simulations.

Los Alamos National Labs' Episims applies graph-based methods to a transportation networks simulation based on population-mobility, land-use, and census data to estimate contact graphs that are assumed to be social networks [17]-[18]. Episims is better than other methods in that it does not assume homogeneous population mixing. But it lets normal, non-attack day transportation patterns drive social networks and agent behaviors, while the reverse is true in reality: agent behaviors drive social networks and social networks drive, even while being constrained by them, transportation patterns. Transportation networks may constrain but do not define social networks, as transportation networks and other infrastructures provide a large number of choices for agents. Episims also models disease spread by disease load, which may lead to incorrect results.

III. BioWar Overview

BioWar is a city-scale spatial multi-agent network model capable of simulating the effects of weaponized biological and chemical attacks [19]. It integrates principles of epidemiology, health science, geography, demographics, sociology, social networks, behavioral science, organization science, and aerosol transport. While BioWar incorporates elements from previous models, it also addresses many of their shortcomings. Recent work has demonstrated that the failure to take the social network and the physical locations of people into account leads to incorrect estimates of disease spread and of response policies because spatial, temporal, and demographic dimensions affect disease spread [5], [20]-[22]. For example, concurrent partnerships affect syphilis persistence [20], bridge populations have influence on the spread of HIV in Thailand [23], concurrent partnerships affect disease transmission dynamics in networks [21], [24], sexual networks affect HIV spread [25], and networks intertwine with epidemiology [22]. BioWar is socially (with social, knowledge, and task networks) and spatio-temporally more realistic than previous bioterrorism attack models.

Major advantages of BioWar's spatial multi-agent network approach include:

- Heterogeneous population mixing, defined by agent and social network characteristics.
- Simultaneous modeling at multiple levels (pathogen, dispersion, first responders, local government officials, knowledge evolution, etc.) without explicit aggregation but with emergence [26].
- Detailed modeling and simulation of individuals and their social networks.
- Locally accurate agent and social network models with good disease and infrastructure models which facilitates high-precision detailed investigation of first-responder plans for bioterrorism response, and fast, detailed, and effective responses in general.

A simulation is only as good as its fidelity to the aspects of the real world it tries to emulate. In BioWar, real data from census, school districts, general social surveys, etc., are used as input. BioWar also generates simulated output that is validated against real data: drug purchases, school and work absenteeism, medical phone calls, doctor visits, ER visits, social network statistics, work patterns, epidemiological (EPI) curves, chief complaints, discharge diagnosis, etc. Major components of BioWar are illustrated below (Figure 1).

The agent model takes as input the social, disease, and environmental data streams. It integrates various models of disease, geography, attack, weather, and communication technology (e.g., health-related website visits and 911 calls). The agent model itself is a finite state machine describing how agents interact, move, are exposed to bioagents, contract disease, manifest symptoms, and seek and receive treatment. The arrows between "privacy" and "output & system compliance" in Figure 1 denote the use of privacy algorithms to ensure the security and anonymity of individuals. The BSS and NEDSS compliant privacy module is being implemented with the cooperation with CMU Data Privacy Lab.

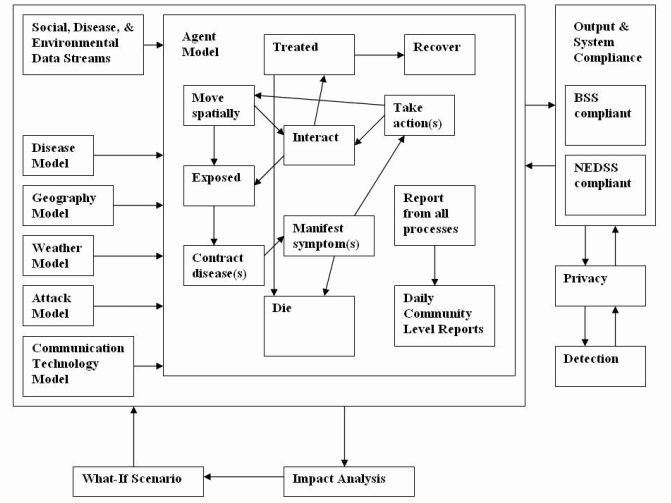

Fig. 1. The design of BioWar. Individual characteristics of the agents, diseases, geography, and general information on communication technology, social, disease, and environmental conditions are used by the agent model to change behavior. Outputs are used to test early detection algorithms and hypothetical what-if scenarios are used to analyze policy. Note that the agent model diagram only represents a small part of the complexity of agent behavior: the complex social networks are not shown.

Agent, disease, geographic, weather, attack and communication technology models have been implemented and used extensively. What-if scenario and impact analysis modules have also been encoded and used to validated BioWar against the SIR (Susceptible-Infected-Recovered) a conventional epidemiological model, for smallpox [27] and against a variant of SIR [28] for non-infectious diseases (in this case anthrax). The detection module uses detection algorithms created by outside groups attempting to detect a bioattack one or more days earlier.

IV. Agent-level Disease Model

The current version of BioWar simulates 62 diseases – 4 weaponized diseases and 58 naturally-occurring diseases – simultaneously in a population. Adding a new disease (e.g. emerging infectious diseases like SARS) is relatively easy: it takes approximately one programmer day. Validating a new disease is harder: it may take days or weeks depending on the disease and the quality of empirical data. We use a symptom-based general disease model. Each disease has its own set of symptoms, timing for disease phases, variations in presentation based on age, gender, and race, and contagiousness. Each instance of a disease infecting an agent is individually represented and progresses through time as the agent goes about his or her daily business. Diseases can propagate through a population, based on probabilistically determined agent risk factors, the transmissibility of the disease, and the spatial and temporal proximity of uninfected agents to infected agents.

Each disease progresses through up to five phases:

1. Incubation: the period of time before the agent begins presenting symptoms.

2. Early symptomatic (prodromal): the period of time during which an infected agent may experience mild or non-descriptive symptoms. Many diseases have no known or identifiable early symptomatic period.
3. Late symptomatic (manifestation): the period of time during which an infected agent may experience severe and/or disease-specific symptoms. In many diseases, this phase may not be distinct from the early symptomatic phase.
4. Communicable: the period of time during which an infected agent may infect other agents. This phase may overlap with the above phases. Noncontagious diseases do not have this phase.
5. Recovery/death: a period of time during which a disease resolves or causes death.

In the current version of BioWar, the length of each phase, except recovery/death, is generally determined using a uniform random distribution with a range provided by expert analysis for background diseases (better distributions may be added when the need arises). Weaponized diseases, however, are treated as a special case and the phase durations are calculated differently [27]-[28]. Recovery and death of an agent, when not affected by treatment, is determined by a Bernoulli process with p equal to the death rate of the disease among untreated victims (again, determined by expert analysis). The duration before death or recovery is likewise stochastically determined.

In constructing our disease model, we used historical accounts of known anthrax releases [29], documents from the October, 2001 bioterrorism attack [30], and disease knowledge bases [31]-[33]. We have also drawn on the experience of other medical expert systems developed to assist in diagnosis to ground our disease model in well-founded medical knowledge representations [34].

A. Risk Factors

Certain demographic groups are more likely to be susceptible to particular diseases than other. These risk factors increase a person's susceptibility to diseases through either host factors or environmental factors to which that person is exposed. In BioWar, risk factors are distributed *a priori* to individuals in the population according to demographic characteristics such as age, sex, race, occupation, and disease prevalence.

B. Symptoms

Symptoms are important in BioWar on two levels. They motivate agent behavior and determine the initial diagnosis of agents entering the medical system. Agents with symptoms self-diagnose, stay home from work, visit their doctor or pharmacist, and change their patterns of interacting with other agents, depending on the severity of symptoms. This symptom-based disease model permits the representation of outliers and stochastic flux (not everyone with the same disease presents the same symptoms). Symptoms are assigned two different measures that influence which symptoms agents feel and how that changes their behavior [34]. The first, frequency, is a qualitative measure of how frequently people with a particular disease will manifest a particular symptom. Frequency is denoted by a number between 1 and 5 that answers the question: "In patients with disease x, how often does one see symptom y?" For example, patients with the diagnosis of anthrax will have a fever frequency of 5 – nearly all patients with anthrax will have fevers at some point in the course of their disease. The second, evoking strength, is a qualitative measure of how frequently a doctor will associate a particular symptom with a particular disease. Evoking strength is coded as a number between 0 and 5. It answers the question: "When you see symptom y, how often would a doctor think the cause is disease x?" For example, fever symptoms are not specific to any one disease – in our disease profile of anthrax, fever is given an evoking strength of 1. However, a widened mediastinum is a more specific symptom of anthrax – in patients who have a widened mediastinum, the possibility of anthrax should be routinely considered thus the evoking strength for this symptom is 5.

C. Agent Behavior-Symptom Relationship

Although individuals get symptoms based on the symptom frequency for the disease that they have, they will actually alter their behavior based on the evoking strength of that symptom. When a symptom is added to a disease, its severity is initialized to the symptom's evoking strength. Then, as the disease progresses, the severity of each symptom is increased randomly each four hour tick by a user-defined value. If an agent is in treatment, the severity is reduced each tick randomly by an amount depending on the type of treatment. Thus, the total severity is determined quasi-randomly based on evoking strengths [34], time, and treatment.

Once an agent is infected, the infection progresses through time via a simple state machine which can be interrupted or altered by external events, such as successful treatment of an agent at a medical facility.

A set of user-specified symptom severity thresholds guides an agent's initial decision to visit a medical facility and the visit outcome is probabilistically determined based upon an agent's demographic profile. The thresholds are limits of the sum of the severities of observable symptoms over all diseases infecting an agent. Hence the true nature of the agent's health status is opaque to the decision model, and the agent only responds to symptoms that can be monitored by the normal human senses. Before the decision model chooses an agent's next care-seeking behavior, the total symptom severity is calculated and measured against each threshold in the following order:

1. Low severity - no effect
2. Mild severity - go to the pharmacy, self medicate (Table I)
3. High severity - go to the doctor
4. Extreme severity - go to the emergency room

These behavior thresholds for going places are currently estimated from empirical visit statistics – say, to doctor offices – and compared to the simulated visit statistics that BioWar produces.

In the future versions of BioWar, we will incorporate detailed rule-based systems for specific symptoms based behavior changes.

TABLE I
SYMPTOM TRIGGERED MEDICATION PURCHASE

	Cough-ing	Sneez-ing	Muscle Pain	Fever	Head-ache	Diarrhea
Cough medicine	✓					
Cold medicine		✓				
Cold/cough medicine	✓	✓				
Cold/cough/fever medicine	✓	✓		✓		
Analgesic			✓	✓	✓	
Anti-diarrheal						✓

D. *Dose-Response Relationship for Weaponized Pathogens*

Currently information about human response modeling for weaponized diseases is scarce. The relationship between the infection probability, illness duration, and onset-of-illness versus inhaled dose were recently published for anthrax, botulism, pneumonic plague and Venezuelan equine encephalitis [35]. At this stage, BioWar takes into account dose and age-of-agent for infection probability for inhalational anthrax following formulas developed by Webb, Blazer, and Buckeridge [36]-[37] while for the other weaponized diseases it uses an exponential model for infection probability.

E. *Noncontagious Disease Submodel*

Our disease model tracks non-contagious diseases. Non-contagious diseases do not have a communicable phase, though some non-contagious diseases can be spread by contact (e.g., anthrax spread by US Mail). Intervention affects disease outcome. If anthrax infection is suspected to be present, this triggers the intervention such as distribution of the antibiotic Cipro. Giving Cipro, in turn, ameliorates the symptoms and possibly cures the disease. For short-duration non-contagious diseases such as food poisoning, outbreaks are randomly generated based on prevalence data. For chronic non-contagious diseases such as angina and diabetes, the initial agent population is afflicted based on known race, gender, and age distributions according to prevalence information. If an agent dies, another agent in the same demographic cohort chosen at random is afflicted.

F. *Contagious Disease Submodel*

Our disease model also allows the representation of contagious diseases. Transmission can occur via contact or air dispersal. When a person comes into contact with the transmission medium, disease transmission occurs with some specified probability.

Agents experiencing disease state transitions are modeled as nondeterministic automata. As past medical history affects these transitions, this is a non-Markovian model. At any time within the duration of a state, a medical intervention can occur and the state can be changed. The state of the disease also affects the medical intervention.

V. DIAGNOSIS MODEL

As previously mentioned, we use a symptom-based differential diagnosis model to obtain information on the diseases infecting an agent who visits a medical facility. Our goal was not to build an error-free diagnosis model. Rather, we use differential diagnosis, as do medical doctors, which allows for the possibility of initial misdiagnosis and the revision of diagnoses with additional information (e.g., lab results). We have based the model on the Internist1/QMR diagnosis model [34], but have augmented the results with probabilistic "switches". As such, our model is not a true computational diagnostic tool, but serves to control the simulator's response to diseases in a simulated population.

Agents self-diagnose on the basis of visible or palpable symptoms. Medical personnel diagnose on the basis of visible symptoms and other information, which can include laboratory tests of varying accuracy (type 1 and 2 errors are possible) and report time. Moreover, doctors and ER personnel take time to file a disease report (up to 8.74 days according to a claim delay data gathered by IBM [38]), delaying institutional realization of a bioattack.

Initial medical diagnosis is simulated based on the apparent symptoms and their evoking strengths. To determine which disease a person has, the groups of evoking strengths of symptoms associated with potential diseases are compared and the highest one is chosen as the diagnosed disease. In other words, the disease most strongly associated with the most severe set of symptoms is chosen. Subsequent diagnosis can update the primary diagnoses based on the appearance of new symptoms and on the results of diagnostic testing. Chief complaints are not necessarily the same as discharge diagnosis, which is consistent with observed hospital performance [39].

VI. TREATMENT MODEL

Diagnosis at a doctor's office results in treatment or ordering of additional tests. If an agent reports directly to a hospital's emergency department, diagnosis results in treatment, tests, or an admission to the hospital. Treatment may not be immediately effective and symptoms vary in visibility and type of testing required for their detection. In the current version of BioWar, recovery after treatment is modeled as a lognormal distribution with a mean of 3 days with a range of 0-10 days for all diseases except anthrax and smallpox. The recovery distribution for anthrax is described in [28], the one for smallpox in [27]. Future versions will have more realistic treatment models for more diseases.

VII. SOCIAL NETWORKS

Epidemiologists have long recognized that groups, organizations, institutions, and the societies in which they are embedded, are complex systems that affect the propagation of diseases through a population. It is only recently that we have had the tools for modeling these systems. These tools include multi-agent computer models and the body of statistical tools and measures that have arisen in social networks [40].

The significance of social networks to contagious disease transmission is obvious. Social networks are also important in delimiting bioattacks using non-contagious microorganisms. While non-contagious bioagents such as anthrax do not spread through social networks, social networks define the exposed subpopulation through co-location of agents at the time and place of an attack.

A. *Representation of Social Networks in BioWar*

In BioWar, each agent is linked to other agents in the simulated population by a set of links (relationships) modeling a social network. Each link is a descriptor of a pair of agents and their relationship type. Agents may be linked unidirectionally or bidirectionally. Relationship types currently implemented are:

- Family (spouse, parent, child, sibling, other family)
- Proximity based (co-worker, schoolmate, group member, neighbor)
- Voluntary (friend, advisor, other)

The relationship types were drawn from the University of Chicago General Social Services (GSS) survey data with the addition of "schoolmate" for younger agents, a population not covered by the GSS [41]. The overall network size and distribution were drawn from Klovdahl's study along with some target numbers for individual relationship counts [2], [3], [42]-[43].

The construction of social networks begins by defining the ego net for each agent based on empirical data on the size and constitution of networks. An ego net is a set of agents with whom an agent primarily interacts. Factors considered during the construction of social networks include target network size for an agent, frequency of relationship type, agent demographics, the agent's customary locations, and agent's state of health.

Table II, drawn from the results of "Challenge 3" version of BioWar, shows the size of constructed social networks for three simulated cities compared to empirical data.

TABLE II
SOCIAL NETWORK SIZE AND RANGE

Social Net Size	Expected from Klovdahl Study	Norfolk *simulated*	San Diego *simulated*	Pittsburgh *simulated*
Average	33	28	28	28
Range	6-97	8-67	6-68	8-86

B. *Agent Interaction*

Agents interact with each other based on BioWar's CONSTRUCT model [44] and on spatial and social network proximities. The core of the CONSTRUCT model encapsulates the co-evolution and emergence of communication and knowledge networks, driven by homophily and expertise-seeking. CONSTRUCT has been validated multiple times using social and organizational data [44]-[45].

The principle of homophily states that people are more likely to communicate with others who are similar to them. Similarity in CONSTRUCT is assessed by attributes such as age, sex, race, prestige, occupation, educational level, social class, belief, culture, interests, and attitudes. The principle of expertise-seeking states that the information-poor are more likely to initiate communication with the information-rich to fulfill their information needs. Moreover, the interaction is mediated by social, family, professional and other networks. BioWar implements multiple agent interactions based on common knowledge and knowledge difference, social network, and random chance.

BioWar implements disease exchange as the result of agent interaction as follows: for each partner of an agent (computed during the interaction step), throw a random die against the transmissibility of each communicable disease affecting the agent. If the die roll succeeds and the partner does not already have the same disease, infect the partner with the disease. Do the same check for the agent for each communicable disease, infecting the partner, and vice versa.

C. *Representation of an Agent*

An agent is represented as a probabilistic finite state machine that has roles such as father, schoolmate, doctor, nurse, teacher, etc. Additionally, an agent has socio-demographic and economic status. An agent is located at specific spatio-temporal coordinates and exhibits behaviors. These behaviors include interaction (communicate, get infected, infect), recreation, going to school, going to work, seeking treatment, purchasing over-the-counter medicines and cold supplies, getting medical information, and moving to other places. Each agent has an ego net and natural biological rhythm (for example, sleeping 8 hours a day). Moreover, an agent can exhibit symptoms and has mental model of diseases. The propensity of an agent to seek treatment is affected by socio-demographic position (age, race, gender, class, etc.), economic status, and severity of perceived symptoms. Note that even if an agent seeks treatment, treatment is not always available, such as when doctor's offices are closed.

D. *Recreational Activities*

The recreation code simulates some of the additional activities people engage in beyond their normal routine (time spent at home, work or school) and medical concerns (time spent with doctors, at pharmacies, or in hospitals). An agent's routine activity is mapped to a number of set locations. The recreation code adds several additional types of recreation venues where agents gather and potentially interact on a more random basis (Table III).

TABLE III
RECREATION VENUES

Recreation Venue	Definition
Stadium	Open air events
Theater	Indoor events
Store	Shopping locations (excludes pharmacies)
Restaurant	Eating locations
Home	Residence

Recreation rates were derived from the 1994 EPA Time Use Survey by grouping activity categories to determine the percentage of the day normally spent in recreation and using the time-at-location data to make a determination as to how much time is spent in each recreation location [46]. Consistent

with the data, much recreation is assumed to occur at the agent's home.

The EPA Time Use data set is sufficiently large to allow some seasonal, weekly and demographic resolution. For the current BioWar implementation, recreation tables were constructed for the four seasons. Each seasonal table contains separate entries for each day of the week, for young versus old agents and for male versus female. Paired tables were employed: one holding the overall recreational probability and the second determining recreational location. Additionally, there are tables for minor and major holidays. Since the Time Use database excluded holidays, the information was derived from annual averages for Saturday.

Because the simulator divides each day into smaller time units (four-hour "ticks"), an adjustment table was also introduced. The adjustment table allows recreational rates to be adjusted to match the normal day cycle: little recreation occurs during hours of sleep and work and more occurs when the agent would logically have free time (for example in the evenings during the week). In order to reflect the empirical data, these tables are set to preserve overall rates: recreation that is deferred is taken later and recreation taken early reduces the chance of recreation later in the day. These tables were derived for stereotypical patterns and are not empirically based.

The recreation code's role is advisory: it indicates that an agent "wants" to recreate, but does not place the agent at a recreational location, that is, recreation is subservient to other more important activities.

VIII. Environmental Models

A. Representation of Weather

The Weather Model determines atmospheric temperature, pressure, and precipitation for the period of simulation. Generated temperature, pressure, and precipitation yearly distributions closely match the historical data published by the National Oceanic and Atmospheric Administration for the simulated regions (San Diego, CA, Pittsburgh, PA, Norfolk, VA, etc.) [47].

1) Wind Representation

The wind model generates wind speed and direction for the period of simulation. Wind is important at and after the moment of the attack, especially when the attack occurs outdoors and the biomaterial is dispersed though wind puff movement. We use a modified Gaussian Puff model of wind dispersion. The assumptions of the model are:

- The dispersed biomaterial is chemically stable and is not deposited to the ground.
- The lateral and vertical variations of the material concentration can both be described by Gaussian distributions, which are functions of downwind distance only.
- Although in the simplest Gaussian model the wind speed is constant with height, our wind model calculates the dependence of wind speed on height.

An essential function of the wind model is to assess the Pasquill atmosphere stability category for the period of an attack. In the absence of detailed meteorological data, we assign a Pasquill atmosphere stability category based on the wind speed and time of the attack but not the sky condition, which is considered to be a reasonable approximation [48].

2) Bioagent Delivered Dose

The dosage inhaled by the agent is calculated using the following equation [49]-[50]:

$$Dose = [QB][\pi u \sigma_y \sigma_z]\text{-}1 exp[-(1/2)(y/\sigma_y)^2] exp[-(1/2)(H/\sigma_z)^2]$$

where Q is the source strength (e.g., number of anthrax spores); B is breathing rate (usually for light work $B = 5 * 10^{-4}$ m^3/sec); u is wind speed in m/sec; σ_y and σ_z are dispersion parameters that are functions of downwind distance x; and H is height of the release in meters. When multiple ground or airborne releases are simulated the total effect on the agent (the summary dosage) is calculated as a sum of dosages from individual releases.

The wind model also includes methods for determining whether the agent is located in the downwind zone and how far the agent is from the point of the release.

Buildings provide some measures of protection to inhabitants from outside spores, so BioWar has a dose reduction factor to describe the building protection for different kinds of building, based on [51]. Building layouts could be used in future versions of BioWar to improve the estimation of delivered dose of both outside and inside attacks by applying more complex calculations.

The generated wind speed and direction distributions closely match the empirical data for the simulated regions published by the EPA and averaged over three years [52]. A comparison between the simulated wind direction data for San Diego and historical 1990–1992 average data is shown in Figure 2. The relative difference between simulated and average historical frequency distribution values is less than 30%.

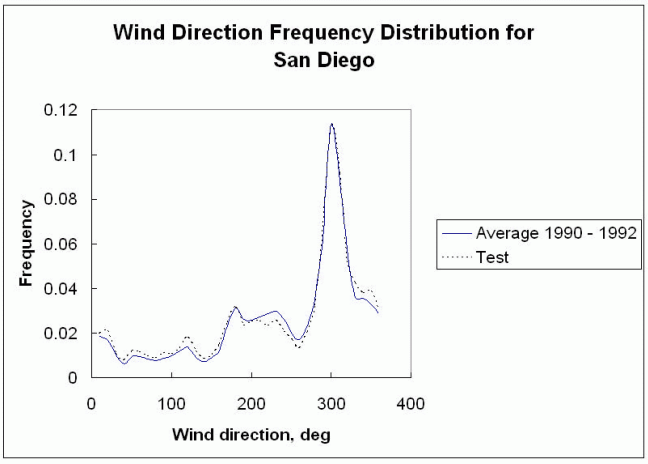

Fig. 2. Comparison between simulated wind direction frequency distribution and average historical data 1990-1992 for San Diego, CA.

IX. Attack Model

BioWar has a flexible attack model for both contagious and non-contagious pathogen release. The model lets attacks be varied by location, date, time of day, agent carrier (airborne, food borne, waterborne, and others), containment (inside or outside of a building), means of attack (land or airborne), delivery type (spray or explosion), pathogen, biomaterial mass, release height and efficiency, and single point or multiple point attack. An example of the attack specification in BioWar:

```
out large anthrax_inhalational 2002/7/4
22:00 25kg .1 300m 1.5km 7;
```

which generates an outside, large, inhalational anthrax attack on July 4, 2002 at 22:00 using 25kg of material for the attack at 10% efficiency, with airborne delivery at an altitude of 300m, distributing 7 bombs along an attack line of 1.5 km. Note that the specification here is only for the attack or weaponized diseases. The BioWar disease model has different specifications for the naturally-occurring background or outbreak diseases.

X. Current Implementation

BioWar is designed as a modular system. A module in the system interacts with other modules via a published interface of methods. A module conceptually corresponds to a BioWar simulation capability, like disease progression and diagnosis. This correspondence is not necessarily one-to-one. The agent model, for example, consists of both an agent behavior module and an agent social network module. This flexibility, which is not possible with a non-modular design, facilitates the rapid development of reliable and more realistic simulation models.

TABLE IV
Data Sources For Input

Origin	Source	Description
USGS	GNIS Database [52]	Hospital, park locations
US Census Bureau	Summary File 1 [53]	Demographics (population, race, age, sex)
	Economic Census [54]	Work, medical, recreation location counts
	Geometry [55]	Cartographic boundaries (region geometry)
NCES	CCD Database [56]	School demographics, locations
	Publications [57]	Student absenteeism statistics
GSS	GSS [40]	Social network characteristics
NCDC at NOAA	NCDC at NOAA [58]	Climate, wind data
Internist 1 [33]	QMR vocabulary QMR evoking strengths	Disease symptoms, diagnosis model
CDC	NCHS Surveys [59]	Medical visit, mortality & morbidity statistics
CDC	Web sites [60]	Disease timing, symptoms

Table IV shows some of the cartographic and other input sources used [34], [41], [53]-[61]. We currently have access to additional data streams which we could not describe here due to confidentiality agreements. Higher fidelity data variants of BioWar are available to health and government authorities with appropriate access privileges.

BioWar is designed to be reasonably portable, and currently runs under Linux, Windows 2000 and XP, and Tru64 UNIX. Most experiments were performed using the Pittsburgh Supercomputing Center (PSC) TCS1 system, which comprises 64 4-way Alpha SMP processing elements (PEs), each with 4GB of RAM and 4 667MHz Alpha 21264A (EV6.7) processors. BioWar's run time scales linearly with the number of agents. A simulation with about 500,000 agents can take 5 or more hours to complete.

BioWar simulator utilizes a tick as the smallest time unit. In the current implementation, one tick equals four hours. The state machines used during a tick of the BioWar simulator are shown in Figure 3.

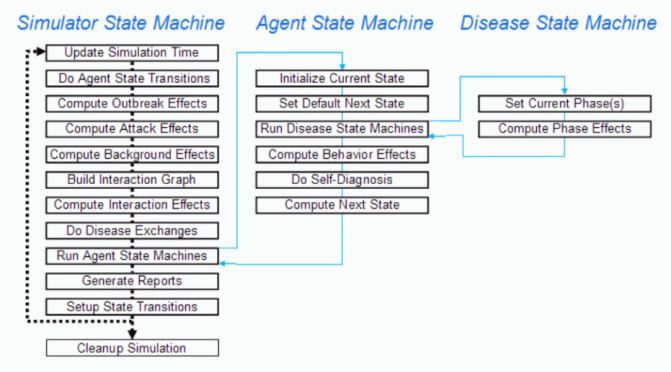

Fig. 3. BioWar State Machines

Integration of multiple models is greatly facilitated by the nature of multi-agent systems. Features and parameters of these agents and modules are defined based on empirical data and knowledge.

XI. BioWar Output Streams

BioWar can be used to present results in the following ways:

- As an additional data layer added to existing background data (injection)
- As a data layer for some outputs (such as ER) and the full data source for other variables (such as drug purchases).
- As a scaled city simulation
- As a complete and full-scale city simulation (for all data not just bioattacks)

BioWar produces output streams including insurance claim data, ER registration data, school absenteeism data, work absenteeism data, and drug purchase at pharmacies data.

BioWar output is generated to conform to NEDSS (National Electronic Disease Surveillance System) which is a set of standards to facilitate the exchange of data for the collection, management, transmission, processing, and analysis of disease surveillance data developed by the Centers for Disease Control. BioWar also generates BSS (Behavioral Surveillance Surveys) compliant outputs. BSS is a set of codified

surveillance guidelines created by WHO and UNAIDS for tracking agent behaviors relevant to the transmission of HIV.

XII. Model Validation

We have validated BioWar outputs against empirical data on school absenteeism, work absenteeism, pharmacy visits, drug purchases, doctor visits, and emergency room visits [19]. Comprehensive validation of a model such as BioWar is, however, difficult to do manually or semi-manually due to model complexity, the significant number of input parameters, model parameters, and output variables, and continuous model augmentation, refinement and development, making automation helpful.

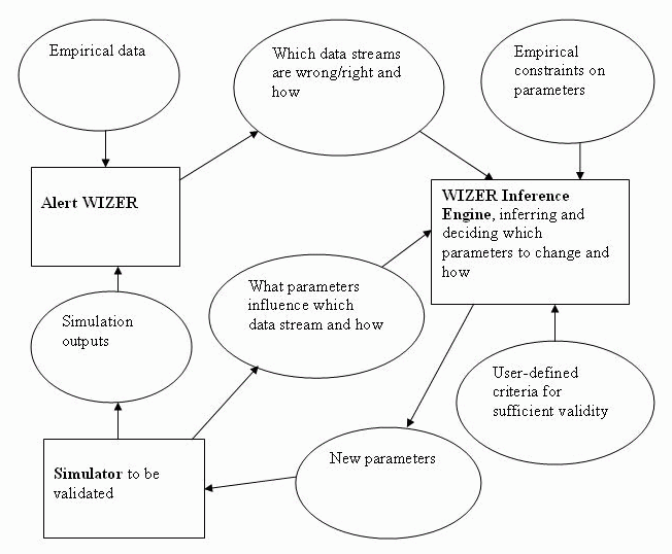

Fig. 4. WIZER Dataflow Diagram

An automated tool – named WIZER for **W**hat-**I**f Analy**zer** – has been designed and partially implemented [62]. WIZER is an integrated inference and simulation engine to do validation and provide explanations. It extends the response surface methodology [63] by performing knowledge-intensive data-driven search steps via an inference engine constrained by simulation, instead of just doing statistical and mathematical calculations. As shown in Figure 4, WIZER checks the outputs of simulation and adjusts the simulation parameters and meta-models based on empirical data to validate the simulator.

In addition, we have validated BioWar against the SIR model (Susceptible-Infected-Recovered), a conventional epidemiological box model, for smallpox [27] and against a variant of SIR [28] for anthrax. In these validation studies, we aligned BioWar and the corresponding SIR model based on their assumptions, model parameters, and simulation results. Empirical data was used to tune model parameters.

Comparison of BioWar against SIR for smallpox outbreaks [27] shows that BioWar and the SIR model produce similar outcomes when model parameters are aligned to the same scenario. For example, for the "base (no quarantine or vaccination)" scenario, shown in Figure 5, BioWar aligns with SIR for cumulative number of infections.

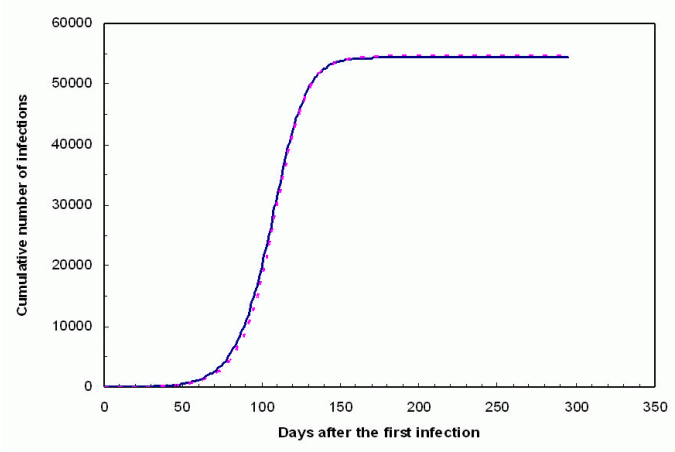

Fig. 5. Cumulative number of infections comparison between BioWar and SIR.

Comparison of BioWar against the IPF (Incubation-Prodromal-Fulminant) model, a variant of the SIR model used for non-infectious diseases like anthrax [28] shows that BioWar produces outcomes comparable to IPF. Figure 6 shows that BioWar generates outcomes comparable to IPF and the Sverdlovsk empirical data for the over-time mortality rate among an anthrax infected population.

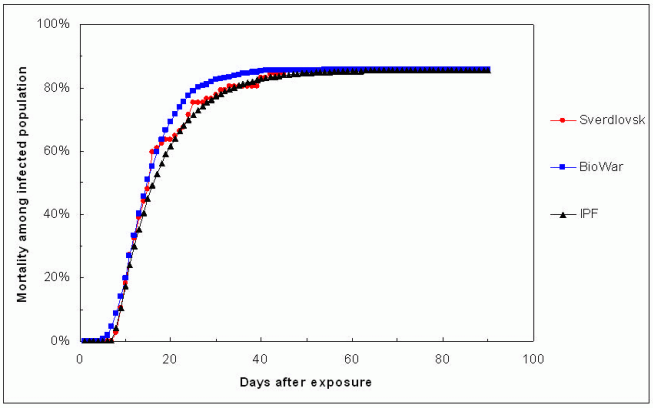

Fig. 6. Mortality comparison between IPF, BioWar and the Sverdlovsk empirical data.

XIII. Sample Runs

We have run simulations for several geographical areas (San Diego MSA, Pittsburgh MSA, Norfolk MSA, San Francisco MSA, Washington DC, and the city of Hampton VA). Many other scenarios can be simulated by BioWar, but we describe just a few examples in this section.

Figures 7-8 contain graphic displays of model output of doctor visits and the number of deaths for an anthrax attack within flu season and a smallpox attack outside flu season in the city of Hampton, Virginia simulated at 100% scale.

When an anthrax attack occurs during a flu season, as shown in Figure 7, it increases the doctor visit rate significantly for a short period of time after the attack. The number of deaths by anthrax is also tightly clustered.

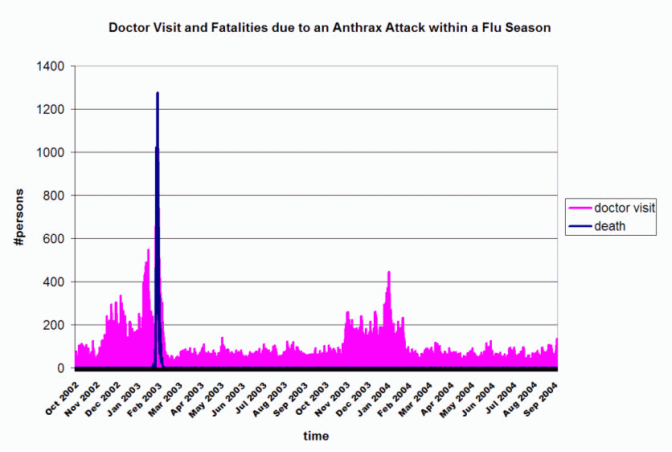

Fig. 7. The number of doctor visits and deaths occurring after an anthrax attack during a sports event at a stadium in the city of Hampton at 4 p.m. of January 25, 2003. 2.5 kg of spores were released with an efficiency of 0.05, infecting 2122 people. This attack happened during flu season.

Figure 8 illustrates a simulated aerosolized smallpox attack on Hampton, VA. Weapons-grade smallpox was released infecting 2%-2.5% of the agents in a locality. The smallpox attack left a much longer footprint compared to the anthrax attack, due to the contagious nature of smallpox. The fraction of infected people who died of the smallpox is also larger.

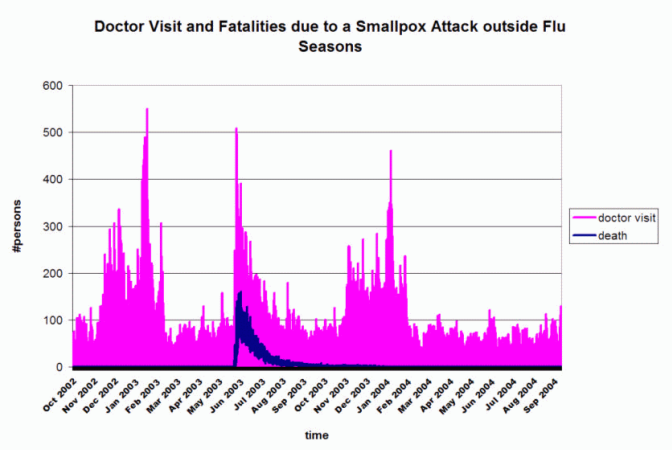

Fig. 8. The number of doctor visits and deaths occurring after a smallpox attack at 4 p.m. on May 26, 2003, in the city of Hampton with a 2%-2.5% initial infection rate. This attack occurred outside the flu season.

For anthrax, which person gets infected critically depends on the release location, the mass of the release and the wind direction. In another experiment, we tried an anthrax attack at a stadium with three different mass of release scenarios: small (150 grams of spores), medium (300g), and large (3,000g). The height of release was 5 meters with an efficiency of 0.05. The attack happens at 4 p.m. in a stadium with the wind blowing at 4.617 m/sec. The simulated population of the city was 148,000. Both the exposed population and infected population vary, as shown in Table V. These are mostly people at the stadium (during a stadium recreational activity) in large measure because anthrax is non-contagious so secondary infections do not occur. For other diseases, such as SARS, secondary infections, particularly in first responders such as doctors and nurses, may occur through the social contacts. The nature of the disease, demographics, available treatment, etc. determines the social contact(s) most likely to spread the disease

TABLE V
ANTHRAX EFFECTS

Data type	Data set	Exposed population	Infected population	Death rate	Infection rate
Empirical	US	Unknown	11	45%	0.10%
	Sverdlovsk	Unknown	77	86%	0.16%
BioWar scenarios	Small	21668	78	81%	0.36%
	Medium	26076	423	85%	1.6%
	Large	28822	2820	83%	9.7%

The reproductive rate for smallpox was estimated using yet another BioWar experiment as shown in Table VI.

TABLE VI
REPRODUCTIVE RATES FOR THREE SCENARIOS OF SMALLPOX ON THREE TYPES OF POPULATION

Scenario	reproductive rate	Types of Population		
		no vaccination	residual immunity	fresh vaccinated
base	R0	4.92	N.A.	N.A.
	R	3.86	N.A.	N.A.
vaccination	R0	2.13	1.28	0.44
	R	1.31	0.53	0.20
quarantine	R0	1.84	1.45	N.A.
	R	1.17	0.38	N.A.

We found that R_0 (the average number of secondary cases in a totally susceptible population infected by one primary case), a value commonly used in SIR model, is not comparable to R_0 in BioWar. In BioWar, R_0 changes for each run. R (the reproduction rate over the entire simulation) is different from R_0 and is calculated as an average reproduction rate over all relevant time steps in a simulation. However, no distinction between R and R_0 is made in the SIR model and R is constant for each run and at each simulation step. This finding implies that, when comparing an agent-based model and the SIR model, modelers should align R_0 (or R) in the SIR with R in the agent-based model since only the average cases are comparable. Aligning R_0 in SIR with R_0 in an agent-based model will provide a misleading comparison.

BioWar can estimate windows of opportunity for attack detection, as shown in Table VII. Our scenarios simulated biological attacks over the town of Hampton, Virginia. The population was about 144,000. Each simulation ran for a year of simulation time starting at September 1, 2002. The simulated attack occurred on October 4, 2002. We conducted 20 runs for each scenario and calculated the mode, mean and standard deviation of W_1 and W_2. The first window of opportunity (W_1) is defined as the time from the occurrence of the attack to the time when the first person shows first non-specific symptoms. The second window of opportunity (W_2) is defined as the time from the attack to the time that the first person is confirmed by diagnosis as having the attack disease. The scenario name denotes the attack disease followed by the number of initial infected agents. For example, Smallpox50 means the smallpox attack scenario with 50 agents infected.

TABLE VII
WINDOWS OF OPPORTUNITY

Scenarios	W_1 Mode, mean, std. dev.	W_2 Mode, mean, std. dev.
Anthrax100	1.7, 1.9, 0.4	5.2, 5.4, 0.8
Anthrax 500	1.2, 1.3, 0.3	4.2, 4.5, 0.4
Anthrax 1000	1.0, 1.0, 0.2	4.2, 4.3, 0.4
Smallpox5	8.3, 9.3, 1.3	13.7, 13.4, 1.2
Smallpox50	7.0, 7.4, 0.7	11.7, 11.4, 0.6
Smallpox500	7.0, 6.5, 0.5	10.7, 10.7, 0.2

The average reproduction rate is around 3.9 for the smallpox cases. In both anthrax and smallpox scenarios, W_1 decreases with the number of initial infections increases and so does W_2. This result is intuitively comprehensible. Since the incubation period of the anthrax is proportional to a lognormal distribution, the earliest time for an agent to show the first symptoms would decrease on average when the sample size (the number of initial infections) increases. Similarly, the earliest time that an infected agent is diagnosed also decreased when the size of the sampling pool increased.

We compared the average doctor/emergency room (ER) visits per person per year with the estimates from empirical data, as shown in Table VIII. The empirical values are estimated from CDC statistics when no known attacks occur.

TABLE VIII
DOCTOR AND EMERGENCY ROOM VISITS

Scenarios	Annual doctor visits per person	Annual ER visits per person
Empirical	Lower bound: 0.415 Upper bound: 1.611	Lower bound: 0.056 Upper bound: 0.232
Anthrax100	0.55	0.35
Anthrax500	0.47	0.29
Anthrax 1000	0.53	0.33
Smallpox5	1.36	0.48
Smallpox50	1.48	0.54
Smallpox500	1.62	0.64

For anthrax simulations, the average number of doctor visits per year is around the midpoint of the empirical bounds and the average number of ER visits is slightly higher than the upper bound. This result is reasonable because most agents with severe symptoms would rush to the ER. However, since the number of infected is relatively small comparing to the total population, the average ER visit per person does not exceed the upper bound by a large amount. For smallpox simulations, the average doctor visits are close to the upper bound and the average ER visits are much higher than the empirical range. Since smallpox is infectious, not only those initially infected need to go to doctors/ER but also agents who are infected over time. It is reasonable that the doctor/ER visits increases more than they do for the anthrax cases.

XIV. DISCUSSION

Several upgrades for BioWar are planned, including:

- Adding physical infrastructure such as road networks and air traffic networks
- Adding organizational response and cost models
- Connecting with real time data streams

While there is much to enhance in the future versions, the current version of BioWar represents a significant advance over other numerical disease models. This includes BioWar's ability to model socially defined mixing and spatiotemporal effects, diverse outputs, multiple levels, emergent properties and unexpected outcomes based on local interactions, and ability to be configured to represent actual cities.

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