Emerging Infectious Disease: A Computational Multi-agent Model

Hong Qin, Alexander Shapiro, and Li Yang

Abstract— **In today's global society there exists a need to understand and predict the behavior of vector-borne diseases. With globalization, human groups tend to interact with other groups that can have one or multiple types of viruses. Currently, there are many mathematical models for studying patterns of emerging infectious diseases. These mathematical models are based on differential equations and can become unmanageable due to many parameters involved. With this in mind, we design and implement a simple spatial computational multi-agent model that can be used as a tool to analyze and predict the behavior of emerging infectious diseases.**

Our novel computational agent-based model integrated with evolution and phylogeny to simulate and understand emerging infectious diseases, which enables us to prevent or control outbreaks of infectious diseases in an effective and timely manner. Our multi-agent spatial-temporal model contributes to epidemiology, public health and computational simulation in several folds: First, our simulation offers an effective way to train public policy decision-makers who will respond to emergent outbreaks of infectious diseases in an appropriately and timely manner. Second, our model has the potential to aid real-time disease control and decision making. Third, our model uniquely takes evolution of viruses into account. Evolution of viruses means their genomic DNA/RNA sequence can mutate and compete for subpopulations of hosts (human, birds/pets). Our implementation provides graphical representation of the results by conducting a set of experiments under various settings.

Index Terms—**multi-agent systems, modeling**

I. Introduction

THIS paper exams the influence on the epidemiological dynamics of pathogen-host interaction by several important factors including density-dependent transmissibility and transmission paths of pathogens, and subpopulation and traveling patterns of human hosts. Typical infectious diseases with contrasting emerging patterns such as Severe Acute Respiratory Syndrome (SARS) and Avian Influenza (Bird Flu) emerged from the Southeastern China can be modeled and investigated from our model. SARS quickly spread globally, whereas the spread of Bird Flu is relatively limited. Their possible factors will be tested in our computational multi-agent based simulation. Our model helps us examine the effect of pathogen transmissibility on epidemics; examine the effect of transmission paths and intervention methods on epidemics. Our simulation is realistic through incorporation of spatial factors and sub-populations. Competition among different virus mutants would effectively "select" the winners. By testing different rules of competitions among viruses and interactions between viruses and different hosts and host subpopulations, we gain insights on how to design better interventions to hold different emerging diseases in check. Our simulation can then be used to compare the effectiveness of different interventions and provide training to public-health decision makers.

Hong Qin is with Spelman College, Atlanta, GA USA

Alexander Shapiro is with H. P. Atlanta, G USA

Li Yang is with University of Tennessee at Chattanooga, TN USA (corresponding author to provide phone: 423-425-4392; fax: 423-425-5442; e-mail: Li-Yang@utc.edu).

II. Multi-Agent Simulation

A. Introduction to Multi-agent Simulation

The propagation of pathogen in a population is a spatial and temporal process. The complex spatiotemporal dynamics of this process is often difficult to be captured realistically by analytic mathematical models. A multi-agent modeling is flexible enough to model the natural complexity observed in both natural and man-made systems. Multi-agent modeling can readily incorporate spatial and local information, and interaction of different entities, and most importantly, can illustrate how group patterns or collective intentionality emerge from individual interactions [11, 1]. An agent is an "intelligent" entity that can autonomously make rule-based operational decisions based on environment and/or histories (temporal information). An agent has local views, which means that there is no agent that has a full global view of the system, and there is no one controlling agents. Agents move around geographically and interact with other agents by which the disease is transmitted. The application of multi-agent model in pathogen-host interaction is also called "microsimulation models" [7].

The work that models pandemic influenza in Egypt [3] uses the Susceptible-Infectious-Recovered (SIR) model and an approach of modeling agents with different states traveling within a single zone landscape. The SIR (Susceptible-Infectious-Recovered) states are based on ordinary differential equations [9]. The Kerman and McKendrick SIR model is defined as follows:

(1)

(2)

(3)

Where t is the time, S(t) is the number of susceptible agents, I(t) is the number of infected agents, R(t) is the number of recovered agents that developed immunity to the infection, β is the infection rate, and γ is the recovery rate. The total population will be defined as N = S(t) + I(t) + R(t). The Kerman and McKendrick SIR model is deterministic and does not study the nature of a population's vital dynamics, including newborns and deaths [3]. The modeling work on pandemic influenza in Egypt uses a real Egypt census data and runs for a number of days. There are agent based models that concentrate less on the presentation of the model and more on the analysis. Those types of simulations require a higher level of understanding of the agent based modeling.

One of those multi-agent systems is the Multi-Agent Model Analysis of the Containment Strategy for Avian Influenza in South Korea model [4]. The Avian Influenza model concentrates on exploiting the data from the 2008 outbreak in South Korea and examines the number of outbreaks on poultry farms by provinces. This is a very specific study and analysis. In comparison, our model is more general but uses similar agent parameters for the simulation, such as infection probability, incubation period, infection spreading distance, and death probability. Those parameters are used with human agents in our simulation, whereas in the Avian Influenza situation they are attributed to poultry agents.

The multi-agent simulation system for H5N1 virus helped to model the human agent in our simulation [11]. The simulation focuses on the Avian Flu and related viruses by testing of containment strategies for rapid response. Their simulation goes one step further by transferring the simulation data to Google Maps. The simulation works on a day to day time slice that shows the number of people exposed to the infectious disease. Then a geographical layout of the region being investigated through the multi-agent simulation model is displayed [11].

Our model allows users to visualize and estimate on how the virus interacts within a single or multi-zone landscape that resembles the real world human interactions, be it a high school or a larger area such as a small town. It also allows for the landscape to be broken into two areas where the agents can travel from one into another, and by doing so, they can infect other agents in the remote zone. Our primary interest is the percentages of recovered agents and agents not infected by the time the simulation ends. Very few simulations provide a simple clean representation of a virus transmission that can be easily understood by a person who has little or no knowledge of how the vector borne disease propagates among people when modeled.

B. A multi-agent model with evolution of the infectious agent

Our simulation environment is defined through a database that contains all the information that is required to create the multi-agent simulation system including information about virus agent, host agent, and landscape of agents. Each agent and landscape has their attributes and functions. The agents follow the function to interact with each other and demonstrate group patterns. There are two types of agents in our simulation: Human and Host agents. The life of the human agent and the virus it can acquire will be based on the rules defined in the state diagram in Figure 1. If the vaccination mechanism is enabled, a user-defined percent of susceptible agents will get vaccinated at the specified interval frequency. If the agent enters a vaccinated state then it cannot acquire a virus. The host agent can only infect the human agent but can take the form of a human host or animal host agent. The simulation will have two landscape modes: single and multi-zone. Agents will be able to travel from one zone to another and spend a pre-defined duration in each other's remote zone before traveling to home zone in the landscape option. Both human and host agents will have a carefully designed random walk algorithm allowing the agents to move within the landscape. The walk of the individual agent will be based on picking a random location on-screen. Instead of using a purely random walk, the direction is changed every time a jittery movement, that does not produce sufficient walking coverage, is encountered [6]. The UML modeling of three classes in our simulation is shown in Figure 2.

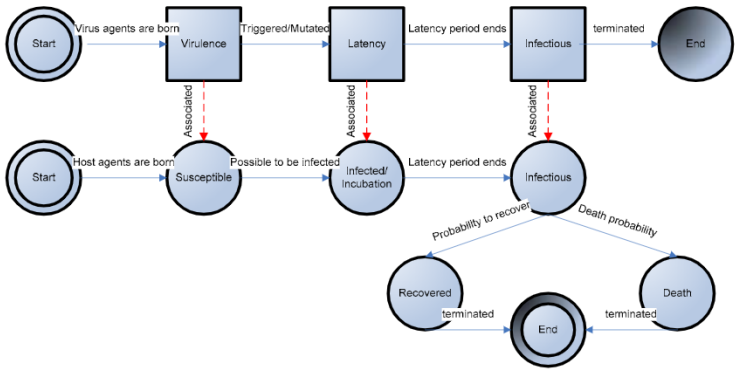

Figure 1 Virus/Host Agent State Transition Diagram

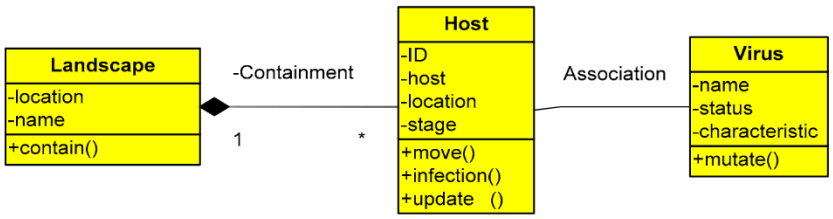

Figure2 Static UML Modeling for our Model

Virus Agents bear characteristics such as "Infectious period", "Latency period", and "Virulence". At the start of simulation, agents of virus should largely be located on non-human hosts, such as pets or birds with "virulence" characteristic. After association with a host agent, i.e. infection, the virus enters "Latency period". The virus agent enters "Infectious period" after given "Latency period". Each agent of virus has its DNA/RNA sequence, which can mutate when the virus transfer from host to host.

Host Agents can be human, birds, and pets. Human populations include individuals that are resistant and susceptible to virus infection. Human individuals in urban areas are more likely to travel long distances, whereas those in rural areas are less likely to travel. An *agent* of host has different attributes also which include *location information*, *moving capacity*, *lifespan*, and *stage*. The states of agent will be "susceptible", "infected/incubation", "infectious", and "recovered/death". An agent of host is born with "susceptible" which is unaffected status. A host agent is likely to be infected when it contacts with another infectious agent with certain exposure and infection rate. Upon infection, the agent is associated with a disease or virus and enters "incubation", but at this stage it is unable to infect other agents. After a given "latency period" of the virus, the agent become "infectious" and can infect other agents. Finally, after an "infectious period", agents become "recovered" and they are immune against the disease or dead.

Landscape of agents can be either towns or cities. Major cities in southeastern Asia will be the main spatial context in our simulation. Landscapes are connected with each other through road and railway networks and airlines.

***Movement functio*n** is one of operations in a host agent represented as method *move()*. A virus agent moves through association with a host agent that travels through transportation networks. The speed of virus spread is related to the "lag" or "incubation" which is the duration a host agent is infected, although not yet showing symptoms. If the "lag" is long, patients are likely to travel longer and further and interact more often with other agents, which will give agents more chances to pass the viruses to more host agents in distant locations. If the "lag" is short, then viruses will grow faster in the host and have more potency for additional infection, but it is more likely to be limited to a local population. We will either simulate virus mutants to randomly adopt these two contrasting strategies, or allow mutants to follow a normal distribution of "lag".

Infection function is one of operations in a host agent represented as method *infection()*. A host agent will be infected upon exposure to infectious hosts given certain infection rate. Infection of virus agents to human agent will be modeled on proximity and virus potency. The chance of a successful infection will be modeled using binomial distribution.

Birth and death function is one of operations in a host agent represented as method update(). Agents of virus can give birth to new viruses. In the scope of this project, the human population will be maintained as a constant, and the birth of human agents will be decided by the number of deaths. Death of human agents will be modeled on the history of virus infection.

Containment function is one of operations in a landscape represented as method *contain()*. The landscape of agents has the ability to respond to various containment strategies that are triggered based upon certain parameters concerning spread of the infectious disease. An example of containment is that a landscape can close their airlines once a specific percentage of agents are infected.

Evolution of the virus agent is a unique feature in our model, which enables us to model the competition among different virus mutants and heterogeneous interaction of viruses to hosts and host subpopulations. The preference of different mutant to different host and host subpopulation can follow a uniform distribution (no preference) or an inverse association (a small subpopulation of host is highly susceptible to certain virus mutants). These different interactions between viruses and host subpopulations are expected to lead to density-dependent emerging patterns. In other words, outbreak should more likely occur in densely populated cities, such as Hong Kong, than other places. Evolution of infectious agent often plays important role in epidemics. In fact, the 2003 SARS outbreak can be completely recapitulated by the molecular evolutionary tree based on the SARS viruses' sequences.

III. Implementation and Evaluation

We develop our multi-agent based modeling using Java and interface with MASON, a single-process discrete-event simulation core and visualization toolkit. The MASON [5] provides us with a simulation console and control console.

The user interface of the simulation consists of two major modules: a Virus Infection Display window and a Virus Infection control dialog window. The Virus Infection Display window, shown in Figure 3, displays both types of agents with icons indicating what agent it is and the states of the agent. The default mode for the single zone landscape is 800x600 pixels. The virus transition states are only relevant to the Human agent. The following are the agents and the states represented by their respective icons:

- Host agent - (grey)
- Animal Host agent - (Animal to Human transmission option has to be selected)
- Susceptible Human agent - (green)
- Vaccinated Human agent -
- Infected-Incubation-Infectious Human agent -
- Recovered Human agent - (blue)
- Not recovered Human agent - (red)

The Human and Host agents can travel to their remote zones and go back to their home zones once the remote zone duration has elapsed. The travel corridor is defined between both zones where the agents do not oscillate too far away along the diagonal path between the two zones. The state, location and properties related to a zone can be monitored when the simulation is paused and a user double clicks on the desired agent to bring up the Inspectors window, Figure 4. Users can adjust the following parameters from the controlling window as shown in Figure 5.

- Single or Dual zone landscape
- Number of agents in each zone
- Percent of human and host agents to travel in dual zone mode
- Human and Host travel rate factors (speed)
- Duration in Remote zone (time steps)
- Duration in Home zone (time steps)
- Infection Distance (pixels)
- Infection and Recovery probabilities (percent)
- Incubation and Infectious times (time steps)
- Human to Human virus transmission
- Animal to Human virus transmission
- Percent to vaccinate (Percent of susceptible agents)
- How often to vaccinate (time steps)
- Simulation Duration (time steps)

There are also real time data that can be monitored and used for simulation analysis. The following data is reported:

- Number of susceptible human agents
- Number of vaccinated human agents
- Number of infected human agents
- Number of infectious human agents
- Number of recovered human agents
- Number of not recovered human agents

This data can also be serialized to a file and used for a specific data processing. Because the simulation is written in Java it can run on any platform, and the simulation can be easily modified or extended as needed.

A series of experiments were conducted using both single and dual zone landscape layouts. The setup for the human to human agent transmission path within a single zone landscape:

- The sample size of susceptible human agents is 499.
- One human agent as the host.
- Duration of the simulation is 5000 time steps.

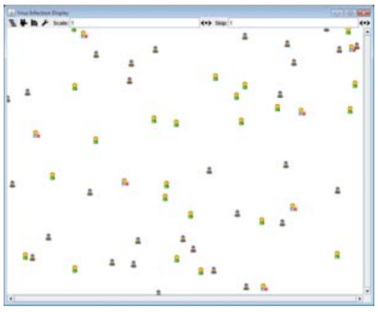

Figure 3 Virus Infection Display window (single zone)

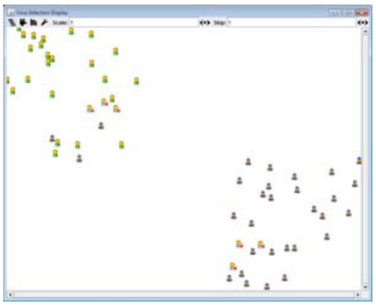

Figure 4 Virus Infection Display window (dual zone)

Experiment 1 shown in Figure 6 monitors the percent of recovered human agents based on the recovery probability. There are four simulation runs and each held the infection probability at constant rate per run at 20%, 50%, 75%, and 96%. Based on the results in Figure 6 we can conclude as the recovery probability increase so does the number of the recovered human agents. As the infection probability goes up per simulation run the graph shifts to the right. Once the threshold of about 60% Infection probability achieved the agents get infected at about the same rate.

Experiment 2 shown in Figure 7 monitors the percent of recovered human agents based on the infection probability. There are four simulation runs and each held the recovery probability at constant rate per run at 20%, 50%, 75%, and 96%. Based on the results in Figure 7 we can conclude that as the infection probability goes up the number of recovered (previously infected) agents goes up. The curves shift to the right as the recovery probability increases.

Experiment 3 shown in Figure 8 monitors the percent of the infected agents based on the virulence duration at 250, 500, 750, and 1000 time steps. From Figure 8 we can conclude as the virulence duration increases the percent of infected agents' increases.

Experiment 4 shown in Figure 9 monitors the percent of vaccinated vs. infected agents where susceptible human agents were vaccinated every 500 time steps. From the graph in Figure 9 we can deduce as the percent of vaccinated agents decreases the percent of infected agents increases.

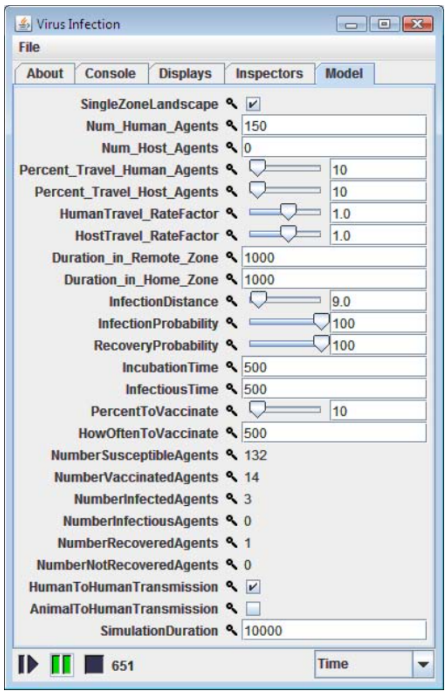

Figure 5 Controlling Window

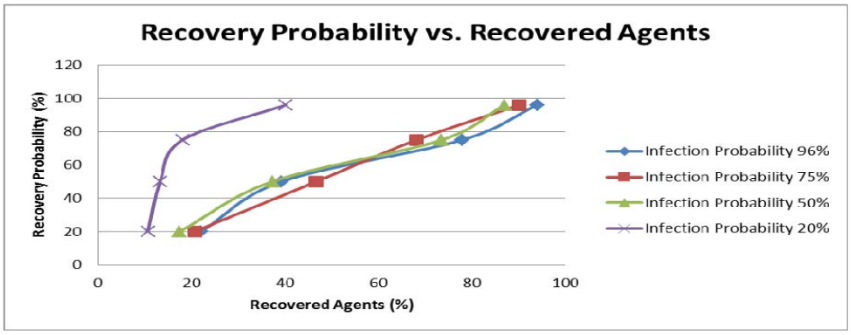

Figure 6 Recovery probability vs. percent of recovered agents

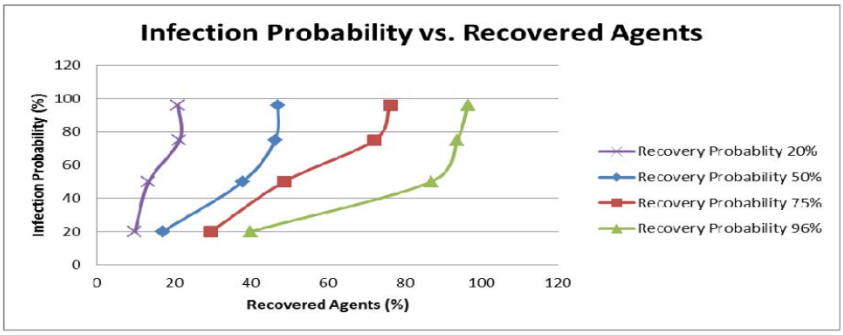

Figure 7 Infection probability vs. percent of recovered agents

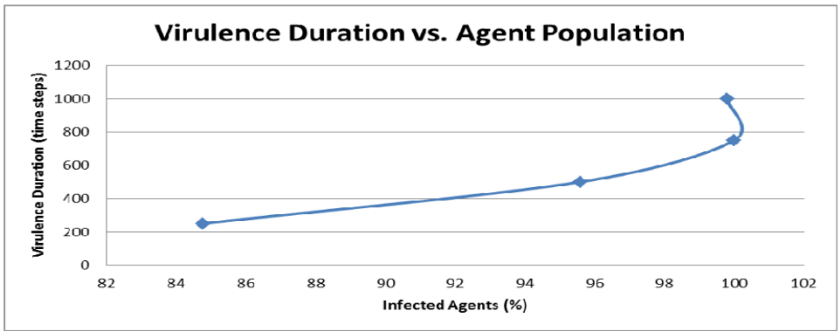

Figure 8 Virulence duration vs. infected agents

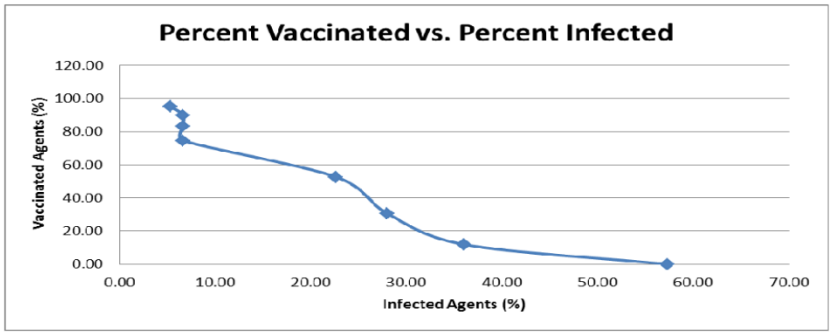

Figure 9 Percent of vaccinated humans vs. percent of infected humans

IV. Conclusion

This paper propose and implement a multi-agent based approach to the study of the transmission path of a vector borne disease that mimics real world human and animal interactions. Our model is able to simulate the development of hypothetical virus model transmission paths between animal to human, and human to human agents in a single and dual mode landscape. The outcome of our model can assist prediction and decision making which is potentially helpful to include countermeasures to control the spread of a specific virus in an environment that is always contains human interaction. The implementation of our model is portable and platform independent as well.

References

[1] Auchincloss, AH and Diez Roux, AV, A new tool for epidemiology: the usefulness of dynamic-agent models in understanding place effects on health, Am J Epidemiol, 168, 1-8, 2008.

[2] Huang, Y. Modeling the severe acute respiratory syndrome (SARS) outbreak in Beijing: an agent-based approach. In Proceedings of the 1st International Conference and Exhibition on Computing for Geospatial Research Application. ACM, New York, NY, USA, Article 36 , 4 pages, 2010.

[3] Khalil, K.M.; Abdel-Aziz, M.; Nazmy, T.T.; Salem, A.-B.M.; , An agent-based modeling for pandemic influenza in Egypt, Informatics and Systems (INFOS), The 7th International Conference on , vol., no., pp.1-7, 28-30 March 2010.

[4] Kim, T., Hwang, W., Zhang, A, Sen, S., and Ramanathan, M. Multi-agent Model Analysis of the Containment Strategy for Avian Influenza (AI) in South Korea, Bioinformatics and Biomedicine, 2008. BIBM '08. IEEE International Conference on , vol., no., pp.335-338, 3-5 Nov. 2008.

[5] Luke, S., Cioffi-Revilla, C., Panait, L., and Sullivan, K. MASON: A New Multi-Agent Simulation Toolkit. Department of Computer Science and Center for Social Complexity, George Mason University. URL: http://cs.gmu.edu/~eclab/projects/mason/, retrieved 2012.

[6] Rao M. D., Chernyakhovsky, A., Rao, V. Modeling and analysis of global epidemiology of avian influenza, Environmental Modeling and Software, Volume 24, Issue 1, January 2009, Pages 124-134, ISSN 1364-8152,.2008.06.011.

[7] Riley, S, Large-scale spatial-transmission models of infectious disease, Science, 316, 1298-1301, 2007.

[8] Roche, B., Guegan, J., and Bousquet, F., Multi-agent systems in epidemiology: a first step for computational biology in the study of vector-borne disease transmission, 2008.

[9] Wolfram Math World. Kermack-McKendrick Model, URL: http://mathworld.wolfram.com/Kermack-McKendrickModel.html, retrieved 2012.

[10] Yang, Z, Computational Molecular Evolution. Oxford University Press, Oxford, 2006.

[11] Yergens, D, Hiner, J, Denzinger, J and Noseworthy, T, Multi Agent Simulation System for Rapidly Developing Infectious Disease Models in Developing Countries, Proceedings of Autonomous Agents and Multiagent Systems (AAMAS), 104-116, 2006.