Modeling the Propagation of Infectious Disease
as a Connected Network

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Abstract

A pandemic is likely to occur in the near future, and this could cause significant disruptions in the human population. Avian influenza is such an example, as it can potentially evolve to transmit from human to human, and spread very fast to become a world-wide epidemic in very a short period of time. In order to prepare for such a disaster and to develop global mitigation strategies for society, the government as well as enterprises needs to understand how widely diseases might spread, and how quickly the magnitude of the infection might grow as well. As the world has rapidly evolved to become a more global chain, the populace contact, social networking and transportation enables diseases to spread more easily than before. In this paper, we present a disease spread model that combines compartmental epidemiological model with a connected network of geographical locations and airports using the system dynamics method. We also quantify how various mitigation actions would affect the spread of disease. This model is intended to be used for firms studying the possible effects of pandemic disease on their businesses. Various scenarios of disease spreads are simulated and examined in this research

Keywords: System Dynamics, Epidemiological Model, Connected Network, Infectious Disease, Pandemic

1. Introduction

In the human history, influenza pandemics have been known to occur every few decades (1918, 1957 and 1968) (Congressional Budget Office 2005). They have caused severe social and economic disruptions. Most people still have a fresh memory of the Severe Acute Respiratory Syndrome (SARS) epidemic outbreak during 2002 to 2003, where several Asian countries and Canada were affected, even though it did not develop into a pandemic. During the last couple of years, the world has experienced unprecedented threat from avian influenza (H5N1 virus) in poultry. The virus could evolve in such a way that it can be transmitted from human to human. Due to this, a potential pandemic outbreak is likely to occur again in the near future.

The social and economic impact of a pandemic has been substantial, as we have seen during the 1918 pandemic and the 2002 SARS epidemic. The developments in medicine and

communication technology may help to reduce the transmission of disease and improve awareness, effectively preparing society in advance. However, increased travels and globally integrated business operations may increase the chances for disease to propagate much faster than ever as people travel more frequently and further than ever before. In fact, the 2002-2003 SARS, although it had a limited number of outbreaks (about 8000 cases worldwide and 774 casualties), made substantial economical and social impacts for many Asian countries and Canada (Hsu et al. 2006).

Pandemic outbreaks are taken very seriously by governments, and private enterprises should also be aware of its effects, because they would negatively impact various aspects of businesses. Many enterprises have their supply partners and markets in various parts of the world, and their workforce also often appear across various geographical regions. The social and economic disruptions resulting from a pandemic would affect business operations in a number of ways, and this could result in substantial loss of revenue for many enterprises. Therefore, it is important for an enterprise to understand the scope and patterns of a pandemic impact on the economy and workforce. In this way, they can develop strategic plans in order to reduce the risk of disaster-related disruptions of their business activities.

In order to estimate the effects of a pandemic and understand disease propagation, we developed a model of disease propagation and mitigations. Specifically, we extended the single node epidemiological model, SEIR (Susceptible, Exposed, Infectious and Recovered) model (Kermack et al. 1927, Anderson et al. 1979), into a connected network model. In order to reflect the reality of this situation, we constructed our parameters based on geographical and demographic data in each region. For instance, population density was factored into the formulation of disease transmissibility. Information on the adjacency of each region with neighboring regions is factored into the disease propagation rate. The information on air travel volume between paired airports was collected and used to estimate the propagation rate between the regions where airports are present.

The government has invested in studying pandemic outbreaks so that it can establish mitigation policies and prepare for the worst-case scenarios (Congressional Budget Office 2005). In our model, the user can specify two categories of mitigation policies for the simulation. For an individual region, the medical care type of mitigation policies can be specified, such as in the utilization of face masks, vaccines, quarantines, the Tami flu, hygiene etc. For the connected networks of regions, government level policies, that can be deployed to prevent disease spreading from one region to another, such as border closing, county closing and airport closing, can be established.

We developed a System Dynamics (SD) model to capture the causal relationships of relevant factors and feedback loops in the target system. The SD model takes 6000 regions and 3600 airports worldwide into account. Government airport closing action, based on threshold on infectious rates, is also modeled through feedback loops captured in the model. The model also has the capability to retrieve the data required for the model such as population density, geographical information of neighboring regions, and air passenger volume between regions from database. The simulation capability of our SD model proves advantageous in examining different scenarios and evaluating the effectiveness of different mitigation actions.

This research will demonstrate the simulation results for several scenarios with a different outbreak origin, extent of disease and with the accompanying mitigation actions. Most of these

simulation results look intuitively correct, while others also provide interesting propagation patterns that may not be obvious at first. Take, for example, the instance of an airport closing that might potentially lead to an undesirable situation by promoting a higher peak of infectious percentage in some regions, or lead to a longer infectious period in other regions.

This work is a part of a global pandemic strategy study that was undertaken to assess the economic impact of the pandemic on a large, globally integrated firm (Chen-Rotzo et al. 2007). This simulation was created in the effort to model the infrastructure, workforce, and the economic impact of the pandemic, and then the supply and demand impact on the firm in various business scenarios. A similar SD model that describes the dynamic impact of a pandemic on workforce absenteeism was studied by Lee et al. (2007).

The paper is organized as follows. In section 2, we review literatures and previous work. Section 3 introduces the networked SEIR model. Section 4 demonstrates some simulation results for certain disease spreading scenarios. Section 5 concludes the paper and discusses further research direction.

2. Literature Review and Previous Work

Epidemiological modeling work originated back to 1927, when Kermack and McKendrick (1927) developed a model with three groups of population; Susceptible population (S), Infectious population (I) and Recovered population (R). Such a model is long known as the SIR model and the mathematical equation is called the Kermack-McKendrick equation. The SIR model has been used widely in epidemiology. This system describes the evolution process of disease affecting a population. In this model, a part of the susceptible population (S) becomes the infectious population (I) as a result of social contacts, and a part of this infectious population (I) recuperates, becoming the recovered population (R). Note that some in the infectious population may die, resulting in certain mortality rate. The SIR model typically assumes that the recovered population will develop permanent immunity to the disease. For certain diseases though, the immunity assumption may not be valid, and the recovered individual could get infected again.

This model can be extended to include an additional group of the population called the Exposed population (E) (Anderson et al. 1979). In this version of the model, a part of the susceptible population could become the exposed population first, and then become the infectious population. Such a model is called the SEIR model, shown in the middle part of Figure 1. A positive feedback loop is reflected in the SEIR model (indicated by the loop sign). A higher Infectious Population may lead to a higher infection rate through social contact. There are many varieties of this SEIR model. For instance, Hsu et al. (2006) extended this model to study the SARS outbreak from November 2002 to July 2003, by adding several other population groups, such as the quarantined and isolated populations. They examined compound effects from intervention measures, including quarantined and public responses.
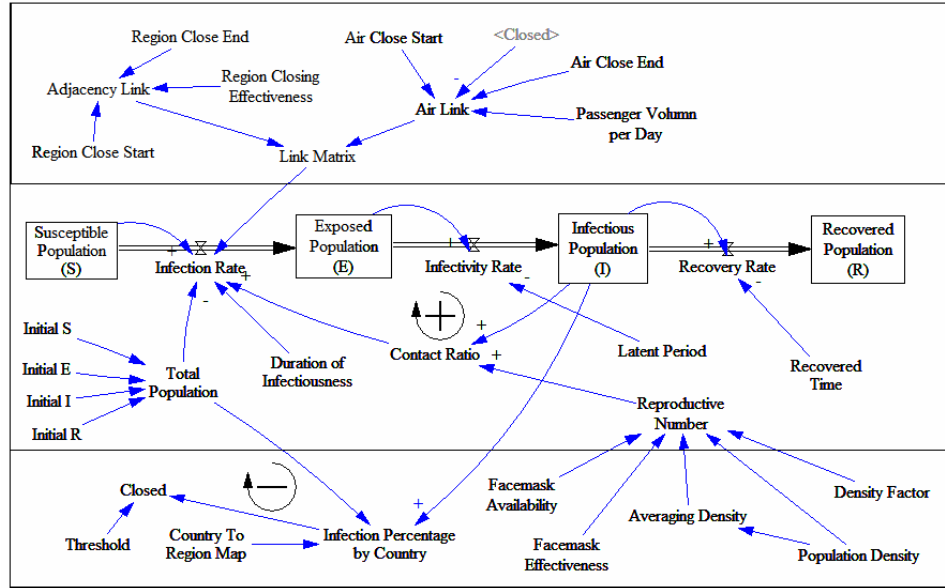
Figure 1: SEIR Disease Spread Model

The models mentioned above are deterministic models and they typically assume homogeneity of populations with respect to the four population categories. There have also been stochastic modeling approaches, and this includes the work by Germann et al. (2006), who introduced a large-scale stochastic agent-based simulation model (EpiCast) to predict the US nationwide spread of disease and to assess various mitigation strategies. Ford et al. (2006) also created a software system and framework called STEM (Spatial and Temporal Epidemiological Model) for modeling multiple populations in geographically distributed locations. This framework is capable of putting an additional model layer to represent the airport connection network and for specifying different characteristics for each region. We developed a light-weight networked model using an SD tool, and utilized available geographical and demographic data. The mitigation strategies are implemented through feedback loops, and they can be established differently by varying regions.

3. Networked SEIR Model

The system dynamics methodology was utilized in the development of our disease spread model. (Forrester 1961, Sterman 2000), and was accomplishing using a modeling tool called Vensim (http://www.vensim.com). Vensim possessed the capability to model multiple homogenous variables as an array, whose elements represent sub-domains. Using this, we separated the world into approximately 6000 regions to differentiate the spread of disease in various regions of the world. Based on the availability of data, the granularity of our model is different for different continents. The model is allocated to the county level in some countries, and the state/province level for other countries, and even the country level in some continents. We assumed that each region had a homogeneous population structure. However, transmissibility would differ from region to region due to varying population density. Also, the spreading of disease from one region to another depends on geographic neighboring among the regions and air transportation infrastructure. In our model, we have included 3600 airports around the world in.

It is important to understand severity of disease in multiple regions. For a single node model, the severity of disease is typically measured in terms of infectious population over the total population, duration of infectiousness and the mortality ratio among the infectious population. Another factor that indicates the severity of a pandemic is the scope of spread, i.e., how many regions, countries, or continents have been affected. The SARS outbreak in 2002-2003 had a relatively high mortality rate (about 10% of the infected population died). However, due to the quarantine measures deployed during the SARS breakout, the infected population was isolated effectively and the scope of the spread remained relatively low (mostly confined to the Asian countries and a few rare occurrences in others, with the total of 29 countries) (Hsu & Hsieh, 2006).

3.1. Networked Model

In order to model the propagation of the pandemic around the world, we extended a single node SEIR model to a connected network model with multiple nodes. Disease propagates along the connections in the network. In our model, the connections represent the people traveling by road or by air from one region to another. Transmissibility of disease in certain regions may vary considerably, as population densities differ. Figure 2 shows a networked model with two nodes. The rate at which the susceptible population becomes the exposed population is affected by the infectious population from both regions, when both regions are connected through either road or air.

In addition to modeling the spread of disease, we also modeled how mitigation actions affect the spread of disease. We included two types of mitigation actions in our model. One type of action, shown on the left side of Figure 2 as Mitigation Action I, could affect the transmission rate of the disease between two regions through the road and air connections, because mitigation actions such as airport closings, border closings, and port closings, could reduce or block the movement of people from one region to another. The other type of mitigation action, shown on the right side of the Figure 2 as Mitigation Actions II, would modify the transmissibility within a region, since those mitigation actions, such as distributing medical supplies, could be deployed independently for each region. This model of disease transmission shown here is applied to all the regions that are connected.
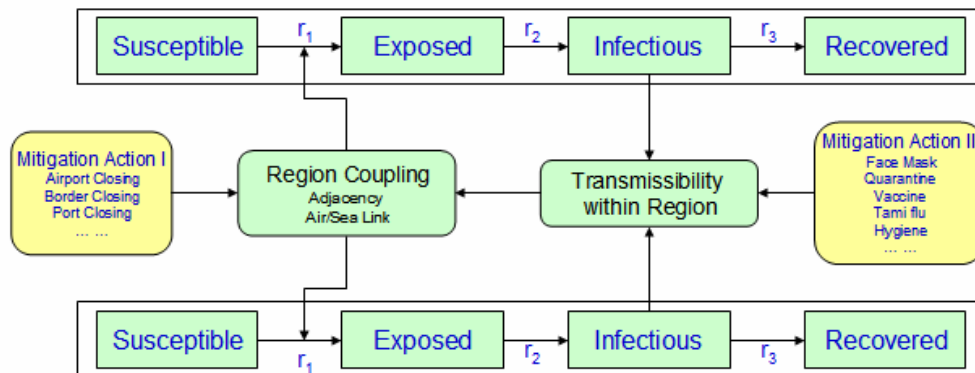

Figure 2: Two nodes SEIR model with mitigation

Similarly, the concept of the two nodes model applies to the general network model. As shown in the Figure 1, the middle section of the figure represents the multiple nodes of the SEIR

process using arraying capability. The coupling among regions is shown in the top section; the link matrix (6,000 x 6,000) represents the quantified connection. For instance, if the entry at [i,j] is nonzero, it means that there exists some movement of people between regions i and j through road and air transportation. We decomposed the "link matrix" into the "Adjacency Link" and "Air Link". An mitigation policy, such as the "region closing" and "port closing", would reduce the "Adjacency Link". Another mitigation policy, such as "airport closing", would reduce the "Air Link". The mathematical formulation which describes the link will be given in Section 3.3. The bottom part of Figure 1 records the modification of the "Reproductive Number", which is related to population density, in each region. Also, medical preventive mitigation actions, like "Facemask" and "Vaccine", affect the "Reproductive Number" in that region. The mathematical formulation quantifying transmissibility change will be provided in Section 3.2. In the bottom part of Figure 1, we also added an additional negative feedback loop to automate the "Airport Closing" mitigation action based on a specified threshold. First, we utilized the "Country to Region Map" in order to aggregate the infectious population and obtained the value of the "Infectious Percentage by Country". If it is greater then the specified "Threshold", we must close all airports going in-and-out of that country (the value of "Air Link" would be modified for some entries).

Since the size of array for representing geographical regions is considerable large, it is impossible to manually enter the data on population and area of over 6,000 regions and 3600 airports into the Vensim model. We must first enter the geographic and demographic data into the database, and then use programming model to retrieve such data and set value for the Vensim model before doing the simulation. Similarly, the SEIR data generated by the simulation is retrieved from a Vensim output file and is saved into the database for further analysis.

3.2. Mathematical Models of Transmissibility

In modeling transmissibility within a region, we first formulate how the population density affects the transmissibility (through the Reproductive Number in our model) as,

$$R_e[i] = R_o * \left(\frac{D[i]}{D^*}\right)^{\lambda}, \quad D^* = \frac{1}{N}\sum_{i \in S_I} D[i] \qquad \text{(Equation 1)}$$

where i is a subscript for the different region; S_I is the set of all indexes of regions with the size of N (6000 in our model, including counties, or states, or countries); $R_e[i]$ is the effective "Reproductive Number" at the region indexed by i; R_o is the original reproductive number, which is defined as the average number of persons effectively in contact by a person during the infectious period; $D[i]$ is the "Population Density" in the region and D^* is the "Average Density" in all considered regions. The exponential parameter $\lambda > 0$ (Density Factor in the lower part of Figure 1) is used to adjust the sensitivity of density on transmissibility. When λ is close to zero, the value of $\left(\frac{D[i]}{D^*}\right)^{\lambda}$ would be close to one and the transmissibility is less sensitive to a population density change.

To account for the influence of the second type of mitigation action (Mitigation Action II), the expression for R_e is further altered to be,

$$R_e[i] = R_o * \left(\frac{D[i]}{D^*}\right)^{\lambda} * \prod_{j \in S_J}\left(1 - E_2[i, j] * C[i, j]\right) \quad \text{(Equation 2)}$$

where j is the index for the second type of mitigation set S_J; $E_2[i, j]$ is for the effectiveness of the mitigation policy for region i for the mitigation action j; and $C[i, j]$ represents percentage coverage (availability) of the mitigation action. $E_2[i, j]$ represents effectiveness of the mitigation action j for region i. Therefore, the third factor in the RHS of equation 2 counts for the compounded effect of the second type mitigation actions. Note that both $E_2[i, j]$ and $C[i, j]$ are indexed by i, since mitigation actions can be applied to each region differently.

3.3. Mathematical Model for Network Connections

In the representation of the influence from different regions, the infection rate r_1 ("Infection Rate" in Figure 1) is adjusted by introducing a $N \times N$ "Link matrix" (see top part of Figure 1) M,

$$r_1[i] = \frac{S[i] * \sum_{k \in S_I} M[i,k] * R_e[k] * I[k]}{T_{se} * P_o[i]} \quad \text{(Equation 3)}$$

where k is an index for region; $I[k]$ represents the infected population in the region indexed by k; $S[i]$ is the susceptible population in the region indexed by i; $P_{own}[i]$ is the population in the region indexed by i; $R_e[k]$ is "Reproductive Number" in region k; T_{se} is the "Duration of Infectiousness" i.e., the time taken for the susceptible population to become the exposed. Without the connection influence (road or air), $M[i,k]$ would be an identity matrix, which contains the value of one for diagonal entries, and the value of zero for non-diagonal entries. Let $P_{con}[i]$ be the total population of regions connected to region i. Then the probability, $p_r[i,k]$, of people traveling from region i to region k would be

$$p_r[i,k] = \frac{P_{own}[k]}{P_{con}[i]} \quad \text{(Equation 4)}$$

Suppose that the daily travel percentage with neighboring regions is $\beta[i]$. In this case, the off-diagonal entries would be

$$M[i,k] = \frac{\beta[i] + \beta[k]}{2} * \frac{p_r[i,k] * P_{own}[i] + p_r[k,i] * P_{own}[k]}{P_{own}[i] + P_{own}[k]} \quad \text{(Equation 5)}$$

The contribution from air transportation is formulated in a similar way. When passenger volume information, $V[i,k]$, is available between regions i and k for one year, we use real data to populate the matrix as $M[i,k] = V[i,k]/365$. For an air connection, we assume a full mesh connection among the hub airports, and the non-hub airports are connected only to the hubs in the same country.

To account for first type mitigation actions (Mitigation Type I), the link matrix M is adjusted by an additional factor as such,

$$M[i,k] = \frac{\beta[i] + \beta[k]}{2} * \frac{p_r[i,k] * P_{own}[i] + p_r[k,i] * P_{own}[k]}{P_{own}[i] + P_{own}[k]} * \left(1 - E_1[i,k]\right) \quad \text{(Equation 6)}$$

where $E_1[i,k]$ represents the effectiveness of road or air closings between regions *i* and *k*. The value $E_1[i,k]$ varies from 0 to 1, with zero representing no closings at all, and one for fully effective closings.

4. Simulation Scenarios and Results

We set up the simulation scenarios which may aid a firm in understanding the propagation of a pandemic disease and the impact of mitigation actions. We simulated a disease starting from a certain region, and some government mitigation policies being applied in these regions.

Due to a globally integrated economy and outsourcing, many companies are interested in the worldwide propagation pattern of a pandemic disease. In particular, many companies expand their financial investment in the Asian market, such as China and India. But compared to most of Europe and the United States, Asian countries are more vulnerable to disease outbreaks.. Based on such concerns, we chose Vietnam as the disease origin country and investigated the spread along network connections via ground and air transportation.

The first postulated scenario is for a mild case of pandemic to occur in which the unmodified reproductive number is relatively small. We also assumed that all airports are open at the time of the pandemic. Figure 3 shows changes of infectious population over time in several regions around world. The infectiousness in various countries outside Vietnam spreads at a later time, depending on the proximity of those countries from Vietnam. The simulation results demonstrated that the magnitude and duration of the infectiousness in various countries are different from country to country because of difference in population density. For Thailand, we treated the country as one region with aggregated country level data and simulated accordingly. The curve of infected population covers longer time span due to the fact that the peak in different regions might not occur at the same time.
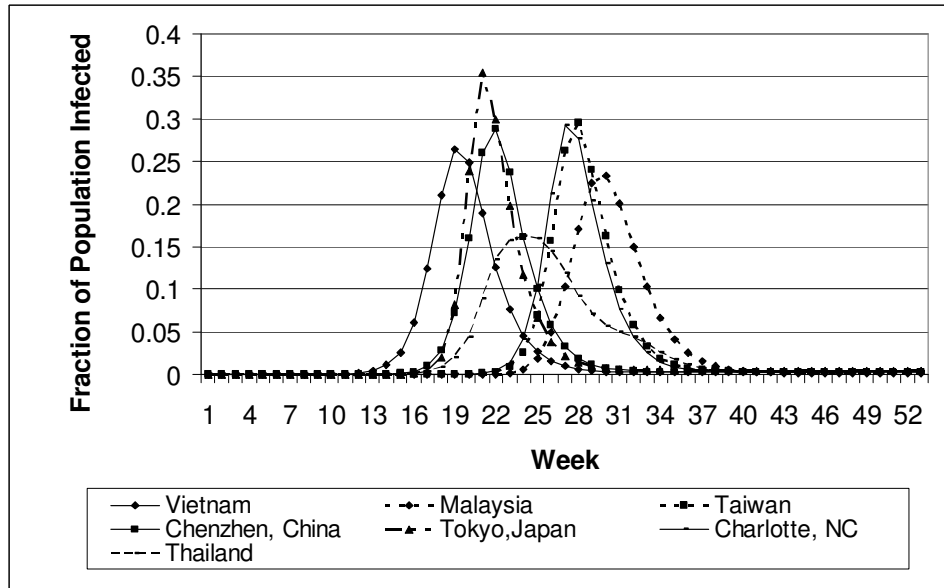

Figure 3. Scenario 1: Mild Disease Seeded in Vietnam, All Airports Open

Note that the spreads along the adjacent link and along the air link have different patterns. For two regions that are farther apart from one another, disease propagation from one to the other might take a longer time, since it passes through several intermediate regions in a sequential pattern. For two regions that are connected with an air link, the global spread would be rapid.. Figure 3 shows that the growth rate in Tokyo is faster than the growth rate in Chenzhen, China, since the latter is mainly affected by an adjacent link.
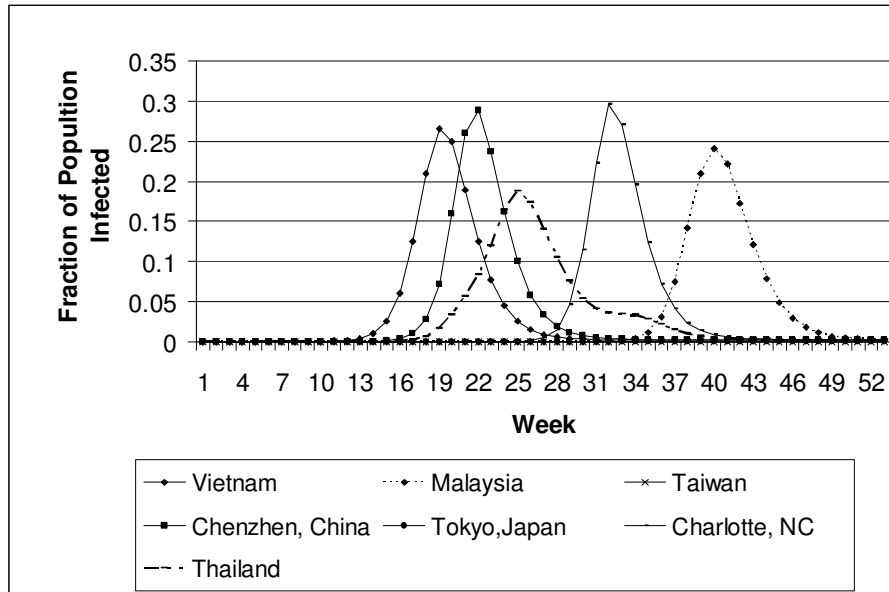

Figure 4. Scenario 2: Mild Case with SEA, Japan and China Airports Closed

The second scenario would also be for a mild case pandemic, but with the airports in southeastern Asia, Japan and China closed. Figure 4 shows the simulation results. In comparing this with the first scenario, the infectiousness curves are similar in shape and magnitude. However, the mitigation actions and airport closings slow down the propagation of the disease from one region to another. The magnitude of the peak is almost same, but the curve is shifted to the right, indicating slower propagation of the disease. Assuming that everything else stays the same, the disease will propagate to other regions more slowly because of airport closings, but as long as it enters, the disease will still cause a infectious population in that region and the magnitude of the infectiousness will be almost the same.

Certain things that we observed from the simulation in the above two scenarios are intuitive, establishing that:
1. The infectiousness in Chenzhen, China does not change significantly, because the airports are closed and traveling between Vietnam and Chenzhen is mainly via ground transportation.
2. Japan and Taiwan do not have a infectious threat anymore after closing their airports, because air transportation is the only means of transportation between Vietnam and these counties. In fact, there are no land connections from those regions to Vietnam and traveling by sea is excluded in our model.
3. Infectiousness in the US and Malaysia occurs at a later time compared to other countries, because even without air transportation, there is still land transportation available

between Vietnam and other countries. Therefore, the closing of airports delays the propagation of the disease to those counties.

In addition, we noticed some rather interesting simulation results that are unexpected for Thailand. The profile of infectiousness for Thailand appears to be quite different from any other region, representing the effect of a connected network structure. Its peak is not too high, but lasts longer, demonstrating a re-bouncing pattern during its decreasing period. The low peak of infectiousness in Thailand is not necessarily related to the lower population density there. The magnitude of infectiousness is actually higher when airports are closed than when they are open. In fact, the formation of these propagating patterns is related to synchronizing and non-synchronizing effects of infectiousness in all the regions that are connected to Thailand. If the peaks of the infectiousness profiles of all the connected regions occur around the same time, the peak of the infectiousness curve of the particular region, Thailand in this case, would occur at a higher magnitude as the connected regions. However, if the peaks of the infectiousness profile of all the connected regions occur at different times, then the infectious period would last longer. It is also possible that the infectiousness curve could have multiple peaks. After closing some airports, the propagation of a disease from one region to other is altered. While some regions are affected through ground connections only, and the others are affected by both ground and air. However, the arrival time would change since the traveling path is different. Therefore, depending on how a region is connected to its surrounding regions, the profile of infectiousness of a particular region with respect to surrounding regions would be in three different shapes; (1) the infectiousness profile is the same as the surrounding regions with certain delays, (2) the infectiousness profile is synchronized with the surrounding regions and amplified, (3) the infectious profile is not synchronized with surrounding regions and is weakened with several peaks.

The fourth scenario describes a severe case of a pandemic with all airports open. In that case, we choose a higher reproductive number, a different recovery time and a latent period. Figure 5 shows a higher magnitude of an infectious population in the same regions compared to Figure 3.
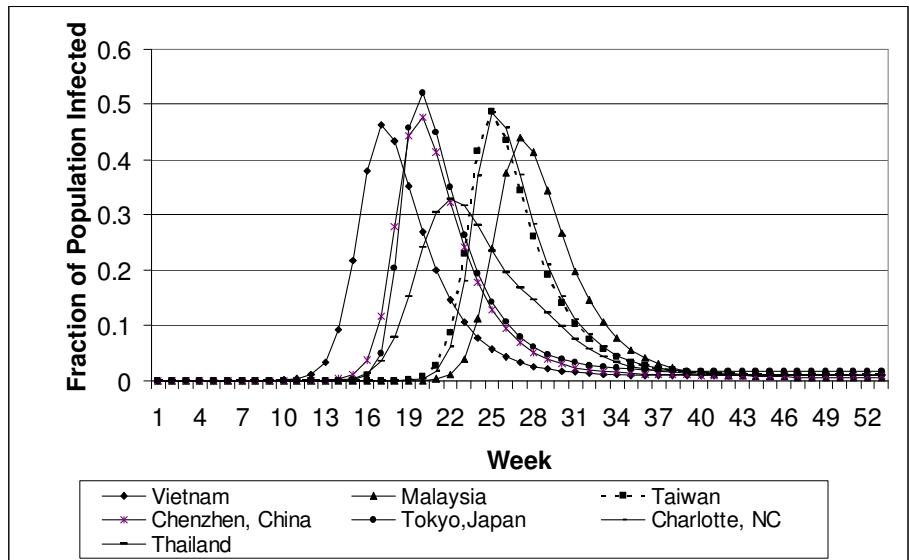

Figure 5. Scenario 3: Severe Disease Seeded in Vietnam with all Airports Open

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The fifth scenario is also used for a severe case pandemic with the airports in southeastern Asian, Japan and China closed. Figure 6 shows results similar to Figure 4, but with a higher infectious ratio.
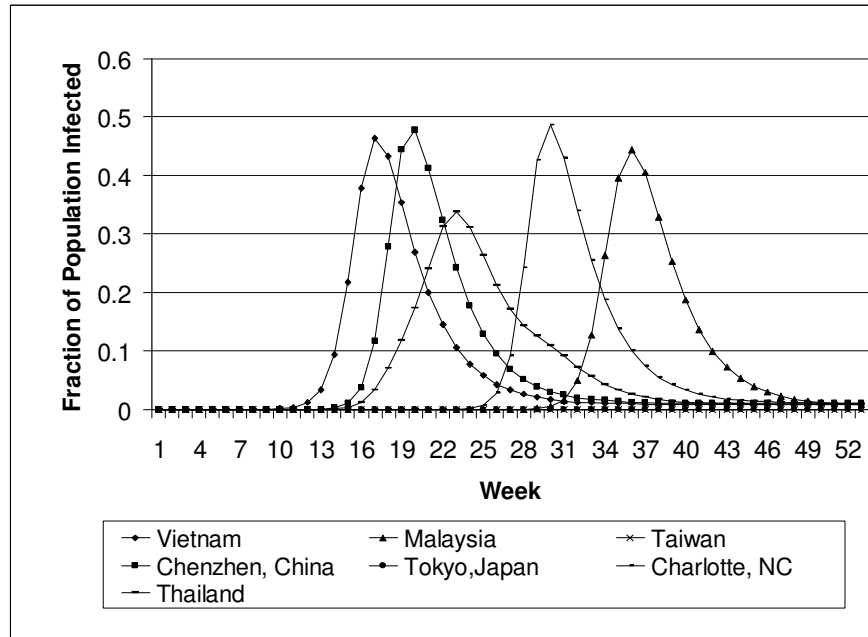

Figure 6. Scenario 4: Severe Case with SEA, Japan and China Airports Closed

We also tested a mitigation policy of closing airports only when a fraction of the infected population reaches a certain threshold. It is found that it is difficult to simulate the conditional closing of airports in SD modeling. When the disease is propagated to some countries before closing their airports, the local infectious growth rate is mainly determined by the social contact there. Unless the infected persons there are quickly identified and quarantined, the disease could quickly spread in the community, even if the airports are closed. However, in the SD modeling, if transmissibility inside a region is the smallest possible number e.g., a single person, the transmissibility of another region which is in contact with the region by air link can be a much smaller number e.g. smaller than a person, which nevertheless would grow and infect other people. This is not a realistic situation, but since this is a continuous model for connection between regions, disease could still spread to another region from a small fraction of a person. It may be more realistic to model the connection by the stochastic or discrete modeling approach, from which it is possible to model the conditional closing of an airport.

5. Conclusion and Discussion

We developed a networked disease propagation model that combines a compartmental epidemiological model with a connected network of geographical locations and airports using the system dynamics method. The heterogeneity among various regions is taken into account through population density. The mathematical model incorporates two types of mitigation actions that would affect either transmissibility in an individual region or propagating the speed of disease from one region to another. This modeling work is a part of a corporate pandemic awareness project (Chen-Ritzo et al. 2007) that is intended to assess the business-side impact of a pandemic. The disease propagation model allows the firm to simulate the pattern and magnitude

of the disease spread and the effectiveness of mitigation actions. The simulation results of the model have been used in determining the financial impact of possible pandemic occurrence on the firm. The model can be further tuned, for instance, to include heterogeneity with respect to time. In fact, transmissibility of a disease can change with time. It is also possible to incorporate infrastructure differences of various regions into the model in order to study how the pandemic risk index (http://maps.maplecroft.com/downloads/PANDEM/index.pdf) would affect the disease propagation. The connection between regions can also be modeled through a stochastic approach. We hope that with this research, government mitigation policies can be further assessed through simulation.

Acknowledgement

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