Modeling Japanese Encephalitis using interconnected networks for a hypothetical outbreak in the USA

by

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Abstract

Japanese Encephalitis (JE) is a vector-borne disease transmitted by mosquitoes and maintained in birds and pigs. An interconnected network model is proposed to examine the possible epidemiology of JE in the USA. Proposed JE model is an individual-level network model that explicitly considers the feral pig population and implicitly considers mosquitoes and birds in specific areas of Florida, North Carolina, and South Carolina. The virus transmission among feral pigs within a small geographic area (<60 sq mi areas) are modeled using two network topologies—fully connected and Erdos-Renyi networks. Connections between locations situated in different states (interstate links) are created with limited probability and based on fall and spring bird migration patterns. Simulation results obtained from the network models support the use of the Erdos-Renyi network because maximum incidence occurs during the fall migration period which is similar to the peak incidence of the closely related West Nile virus (WNV), another virus in the Japanese Encephalitis group (*Flaviviridae*) that is transmitted by both birds and mosquitoes. Simulation analysis suggested two important mitigation strategies: for low mosquito vectorial capacity, insecticidal spraying of infected areas reduces transmission and limits the outbreak to a single geographic area. Alternatively, in high mosquito vectorial capacity areas, birds rather than mosquitoes need to be removed/controlled.

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Dedication

I would like to dedicate this report to my beloved parents, Md Abdul Hakim and Shamsunnahar for their unending support and love and for always being supportive about my decisions. I would also like to dedicate this to my sister Latifa for being the source motivation and strength during moments of despair and discouragement.

Chapter 1 - Introduction

1.1 Overview of Japanese Encephalitis

Japanese encephalitis (JE) is a vector-borne viral disease endemic throughout majority of Asia and Pacific [1]. An estimated three billion persons live in JE endemic countries [2] and number of cases are around 30,000-50,000 per year [1]. The disease can result in irreversible neurologic damage among infected humans. An estimated number of human deaths were 10,000-15,000 in 2002 [1-3]. Japanese Encephalitis virus is transmitted by mosquitoes (mainly *Culex* genre) while pigs and wading ardeid birds (herons, egrets, bitterns, etc.) are respectively the reservoirs and amplifying hosts [1–3]. *Culex tritaneorynchus* and a number of zoophilic mosquitoes as *Cx. gelidus* are main vector species for JE transmission. Humans and horses were found to be dead-end hosts [3]. Introduction of JE to a new geographical location occurs via imported infected pigs, migrating infected birds, or wind-blown infected mosquitoes [4]. Local mosquitoes can acquire the infection while feeding on infectious birds. Infected mosquitoes can then transmit the virus to other hosts (birds, pigs, humans, etc.) when feeding again. Pigs are amplifying hosts of the infection because they act as reservoirs for the disease, showing no signs of viremia but potentially infecting susceptible mosquitoes. In countries with endemic JE infection, such as Southeast Asia and Pacific (mainly India, China and Thailand), pig farms are mainly outdoor and vulnerable to mosquito feeding [6]. These countries also typically have extensive rice cultivation which provides a breeding ground for *Culex* mosquitoes [7, 8]. The proximity of pigs and mosquitoes makes JE a major threat to humans and horses in these regions of the world [9]. However, where pig husbandry has improved through collective pigsties, urban mosquito species, such as *Cx. quinquefasciatus*, have replaced paddy field breeding species (J.P. Gonzalez, unpublished data) [10].

Japanese Encephalitis is prevalent year-round in tropical regions (Bangladesh, India, Nepal, etc.), with a periodic peak in summer [11] while widespread in temperate regions (Japan, China, Taiwan etc.) only in summer months when the abundant mosquito population coincides with the rain and large numbers of outdoor pigs [12]. Transmission of JE in temperate regions such as the United States will have a slightly different transmission cycle than demonstrated in Asian countries. The United States contains two types of pigs: farm and feral [13, 14]. Pig farms here are typically indoors, preventing a majority of insect bites to animals inside these farms [15]. Feral pigs, however, are becoming a growing concern in the United States as they increase in number and geographical span, thereby can significantly contribute to JE transmission [16]. Feral pigs primarily reside in wooded areas in proximity to mosquitoes and wading ardeid birds. Local birds and pigs can move within a radius of approximately 10–60 sq mi [16] and the *Cx.* mosquito has a large flying range up to 4.6 sq mi [17]. Therefore, JE pathogen can rapidly spread up to 10–60 sq mi area in favorable conditions. These areas often overlap, resulting in the infection spreading to a larger area, which can create dangerous conditions in the United States.

1.2 History of Mathematical Model of JE

Mathematical models are useful expressing the spatiotemporal spreading of any pathogen. Mukhopaddhay and Tapaswi (1994) [18] proposed a Susceptible-Infected-Recovered-Susceptible (SIRS) model of JE spreading in a constant reservoir and human population. Each population was divided into three compartments — susceptible, infected and recovered. Ghosh and Tapaswi (1999) [19] proposed a similar model but with variable human and reservoir population. Naresh (2009) [20] proposed a model claiming environmental factors discharged from human population increase reservoir and vector growth rate due to unhygienic conditions which greatly impact JE

spreading. Variable population sizes and disease-induced mortality were considered in this model. Mosquito population were explicitly considered here through carrying capacity and differential infection rate from reservoirs and humans. Agarwal (2012) [21] demonstrated a similar model of Naresh et al. for analyzing effects of media-created awareness regarding the spread of JE. These are important articles on JE modeling but not enough to determine the most important factors to include in the model. Most JE models include human population, which doesn't have an impact on the spreading process for being the dead-end hosts.

The incidence of JE has not been reported in the United States, but this pathogen belongs to the *Flaviviridae* genre, the same genre of the West Nile virus (WNV) [22]. Both these pathogens have a similar transmission cycle, which includes birds and mosquitoes [18]. The occurrence of WNV in the United States generated extensive research activities on its incidence data and transmission. Epidemiology of WNV and incidence data are useful for understanding the hypothetical introduction and incidence of JE in the United States. Therefore, the inclusion of WNV can be very useful to consider various factors in our JE model.

Numerous nonlinear differential equation models —similar to those of JE— are available for WNV. Several models have been proposed based on the contribution of birds to the WNV transmission cycle. Rappole (2006) [23] modeled local and migratory birds spatially to understand their effects of on WNV spread. However, their results were not consistent with data from migratory birds but were in alignment with data for local birds. Some other models, however, showed that the migratory pattern of birds coincides with the spread of WNV in the United States [24, 25], leading to positive and negative opinions about the importance of migration in the spread of WNV. Therefore, although some researchers deny that migratory birds contribute to the long-distance spread of pathogens, pathogens are likely to be transferred to new, distant locations via

them. Therefore, local and migratory birds as local and long-distance dispersal vehicles, pigs as amplifying hosts, and mosquitoes as vectors are three important species to be considered in JE models. Humans and horses are dead-end hosts and do not participate in the spreading process, therefore, are less important and may be excluded from consideration. All proposed compartmental models of JE have a vast number of parameters. Therefore, even if the most important populations are selected and accurately compartmentalized, model parameters must still be precisely selected. However, accurate estimate of these parameters is challenging and prone to large errors in practice.

1.3 Motivation

The incidence of JE has not been reported in the United States, but this pathogen belongs to the JE group, the same group of the West Nile virus (WNV) [22]. Both these pathogens have a similar transmission cycle, which includes birds and mosquitoes [26]. The occurrence of WNV in the United States generated extensive research activities on its incidence data and transmission. Epidemiology of WNV and incidence data are useful for understanding the hypothetical introduction and incidence of JE in the United States. Therefore, careful observation of WNV epidemic models in the USA plays a major role in finding important factors in our JE model.

The literature on JE mainly focuses on Southeast Asia and Pacific where the virus circulates endemically as both a chronic risk in the south and outbreak hazard in the north. However, due to differences in mosquito vector species, and host species, an outbreak in the United States of America will likely have a different epidemiology. Our goal is to examine likely JE transmission along the north-south bird migration route on the east coast of US in the event of accidental or intentional introduction. Our disease model will elucidate the role and key interactions between various native reservoir populations (insect, avian, and mammalian) which may be involved in the

pathogen transmission of this exotic virus in the US. Possible mitigation strategies will be tested to determine the most likely to reduce pathogen spread between geographic locations.

1.4 Our Contribution

Our modeling approach is novel in its individual-level realization of feral pigs with mosquitoes and birds as transmission medium. Contact network among feral pigs within each location are created with two homogenous network topologies- Fully connected and Erdos-Renyi. However, we use a heterogeneous contact structure among local feral pigs and distant feral pigs. This heterogeneity in the contact among local feral pigs is reflected using different pathogen transfer rates from infected to susceptible pigs. Therefore, well-known meta-population approach is not suitable for our network model. Heterogeneity in the contact structure necessitates an individual-level model to describe the epidemiology of JE. Our model being the individual-level, has the flexibility to incorporate the heterogeneity in the network topology when specific data is available about contact structure among individual feral pigs.

Simulation results from the model predict the maintenance of JE pathogen among birds once introduced via a migratory bird even in the absence of feral pigs which eventually results in human incidences. The number of humans infected with JE is comparable to WNV cases among human in our selected location. An effective mitigation strategy against JE is deduced from simulation results of our model. JE transmission can be reduced by lowering mosquito abundance, but both mosquitoes and birds need to be limited/controlled to prevent pathogen spread to distant locations especially in areas of high mosquito abundance.

Chapter 2 - Materials and Methods

2.1 Model

We develop a model for a scenario of JE epidemiology in the United States in which only one population—feral pigs in three spatial locations — is represented at the individual animal level via a connected network. Our simulation model uses a generalized epidemic modeling framework (GEMF) [27, 28] developed by the Network Science and Engineering (NetSE) group at Kansas State University. We carry out extensive simulations, varying parameter values to determine their effects on the overall number of infections (total number of pigs infected) and to relate them to disease dynamics. Model scenarios that included fall and spring migration periods of birds are considered for each of following two network topologies: locally fully connected and locally Erdos-Renyi. These topologies are used to create links among feral pigs within an individual location while inter-location links are created with a probability which ensured, at least, one link between them. These networks are referred as locally fully connected and locally Erdos-Renyi in subsequent sections of the report.

To model JE transmission in feral pigs, we consider a spreading process of a pathogen among N nodes, where N is the total number of pigs in three selected locations. Each node can be in one of three compartments: susceptible, exposed, and infected. We represent individual pigs as nodes in a network; the number of nodes in the network is equal to the pig population size, N. Links among nodes represent the possibility of pathogen transmission from an infected pig to a susceptible pig by mosquito bites. These links were created according to three processes:

(i) from an infected pig to a susceptible pig via mosquito

(ii) from an infected pig to a susceptible local bird and then from that infected bird to a susceptible pig

(iii) from an infected pig to a susceptible migratory bird and then from that infected bird to a susceptible pig in a distant location.

All transmissions occur by local competent mosquito blood feeding.

The role of mosquito population in JE transmission to pigs is expressed by a parameter (β_1) which is the vectorial capacity of focal putative US mosquito vectors. Vectorial capacity β_1 is given as $\frac{ma^2 p^n b}{-\ln(p)}$, where m is mosquito vector density with respect to the host, a is the daily probability of the host being fed upon, p is the probability of daily survival, n is the length of extrinsic incubation period in days, and b is vector competence (proportion of mosquitoes able to transmit JE) [29, 30]. Transfer rate β_2 is dependent on β_1 because this pathogen transfer also occurs via mosquitoes but the inclusion of birds made it different than vectorial capacity (β_1). Here, β_2, is expressed as $r\beta_1$, where r is the local bird's contribution to pathogen spread with respect to the pig density. We refer r as bird community parameter which is a nonnegative parameter with a maximum value of 0.5 because transmission requires a minimum of four feedings when involving birds (pig – mosquito-bird–mosquito-pig) compared to two feedings without them (pig –mosquito -pig). When the bird population has an equal size to the feral pig population in a location, then the maximum value of r is possible. If the bird population exceeds the pig population, then the probability of an infected bird being bitten a second time decreases because alternate bird and pig hosts will be plentiful decreasing the probability of a second feeding (host saturation). Consequently, r decreases from its maximum value of 0.5 if the bird population is more or less than the pig one. For our simulations, three different values of r for the bird community parameter are used: r=0.15 (low bird numbers and species diversity), 0.3 (medium numbers and species diversity) and 0.5

(high numbers and a diverse bird community). This node transition graph of *SEI* model of JE in the feral pigs is shown in Figure 2.1 with all transition parameters.

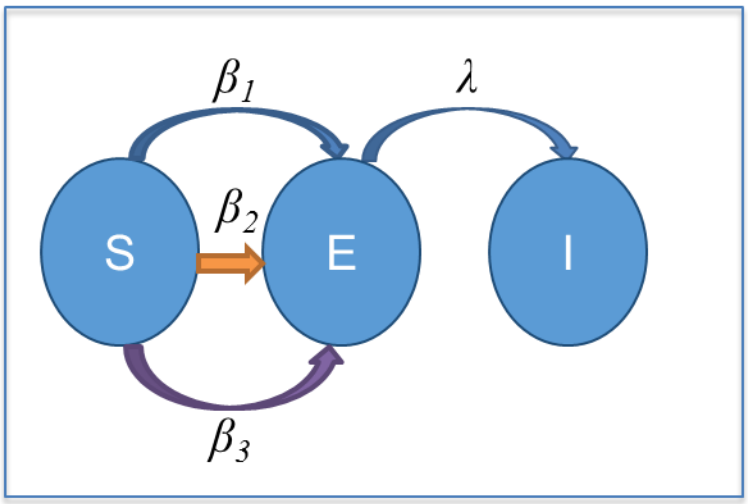


Figure 2.1: The SEI model of JE. Three different transmission rates from susceptible to exposed are indicated with different colors.

As three distant geographic locations are considered in this model, viremic migratory birds are the only means of inter-state pathogen transfer within our simulation period of a single migratory season (90-day). However, a number of conditions are necessary— a bird must become infected in the first location, travel to another location while remaining viremic and spread the infection to mosquitoes. However, no exact method is available to determine the probability of the occurrence of this event, but this is crucial for long distance spread of JE pathogen. This long distance pathogen transfer occurs with a rate β_3, which is dependent on β_2 of the beginning and ending or staging point of the migration and the number and diversity of migratory bird's species in the origin location.

However, pathogen transmissions occur only if a sufficient number of JE-competent mosquitoes bite the infected pig and, after an appropriate period of viral replication in the mosquito, feed on a susceptible pig. Infection processes are statistically independent, therefore, the transition rate for

a susceptible node to the exposed state is the sum of transfer rates times the number of infected neighbor nodes Y_i. The total rate at which an individual pig can become infected is proportional to the infected individuals in the neighborhood and the population size (or density) of competent mosquito vectors. The exposed compartment represents the delays for a susceptible individual to become infectious. An exposed node then become infectious with a rate λ. λ=0.4 day^{-1} is invariably used for all simulations in this report as pigs take 1-4 days to become infectious once exposed to pathogen.

In the Susceptible-Exposed-Infected (SEI) model based on GEMF, infection processes are independent Poisson processes. The node-level Markov process for node i, i = 1, 2,... N, is expressed as

$$Pr[x_i(t+\Delta t)=1|x_i(t)=0, X(t)] = \beta_1 Y_i^{int} \Delta t + \beta_2 Y_i^{int} \Delta t + \beta_3 Y_i^{ext} \Delta t + o(\Delta t) \ldots\ldots\ldots\ldots (1)$$

$$Pr[x_i(t+\Delta t)=2|x_i(t)=1, X(t)] = \lambda \Delta t + o(\Delta t) \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots (2)$$

where x_i = 0, 1, 2 corresponds to node i being in the susceptible, exposed, infectious states, respectively. Value $X(t)$ is the joint state of all nodes—the network state at time t. Yi^{int} denotes the infected neighbors of node i within the same location, while Yi^{ext} denotes the infected neighbors in distant locations. GEMF considers the spreading process of pathogen among our N nodes which can be in three (i.e. S, E, I) different compartments. Modeling starts with a simple node level description of the underlying stochastic processes presented in equation 1 and 2, where nodes are transferring through different compartments with different transition parameters (β_1, β_2, β_3, and λ). An Individual-based model is one of a class of computational models for simulating the actions and interactions of the autonomous individual with a view to assessing their effects on the system as a whole. In these models, the characteristics of each individual (i.e. feral pigs) for our model are tracked over time. The simulation is event-based and stops when the number of events or the

simulation time reaches a maximum value. As the simulation is stochastic, therefore we iterate the GEMF for 90 times and take the average of them for each realization of the process in this paper.

2.2 Network Structure

Our network consists of three spatially separated locations: Miami-Dade County in Florida, Carteret County in North Carolina, and Charleston County in South Carolina. These three counties are selected because they provided WNV incidence data [31], have an abundance of feral pigs [32], the highest number of observed bird's species [33], and proximity to coastal areas.

Locations are selected from three states to encompass a wide range of variability in weather and habitat. Within each location, we consider a small geographical area of 60 sq mi or less as feral pigs roam approximately 10-60 sq mi in search of food [11]. Florida contains more feral pigs and ardeid birds than the other two locations. Birds and mosquitoes are highly variable from season to season and throughout the year, therefore, selection of the appropriate time frame to simulate is essential for accurate epidemiological estimations. Mosquitoes are abundant in the late summer (June-July) and early fall (August-September), crucial seasons for the simulation as bird migration also occurs within this time period. Spring migration is northbound and takes place at the end of the spring and beginning of the summer (April-June). At this period, there is an abundance of birds migrating from the FL location to SC and NC locations but lower mosquito abundance as it occurs before late summer—summer being the peak time for mosquito abundance in all locations. Fall migration, however, occurs during late summer and early fall (July-September), coinciding with an abundant mosquito population. This time frame provides an abundance of mosquitoes, resident birds, and migrating birds in all three locations, which are crucial factors in long-distance dispersal

and local transmission of JE. The relative abundance of mosquito during the different time period in three of our selected locations are presented in Table 2.1.

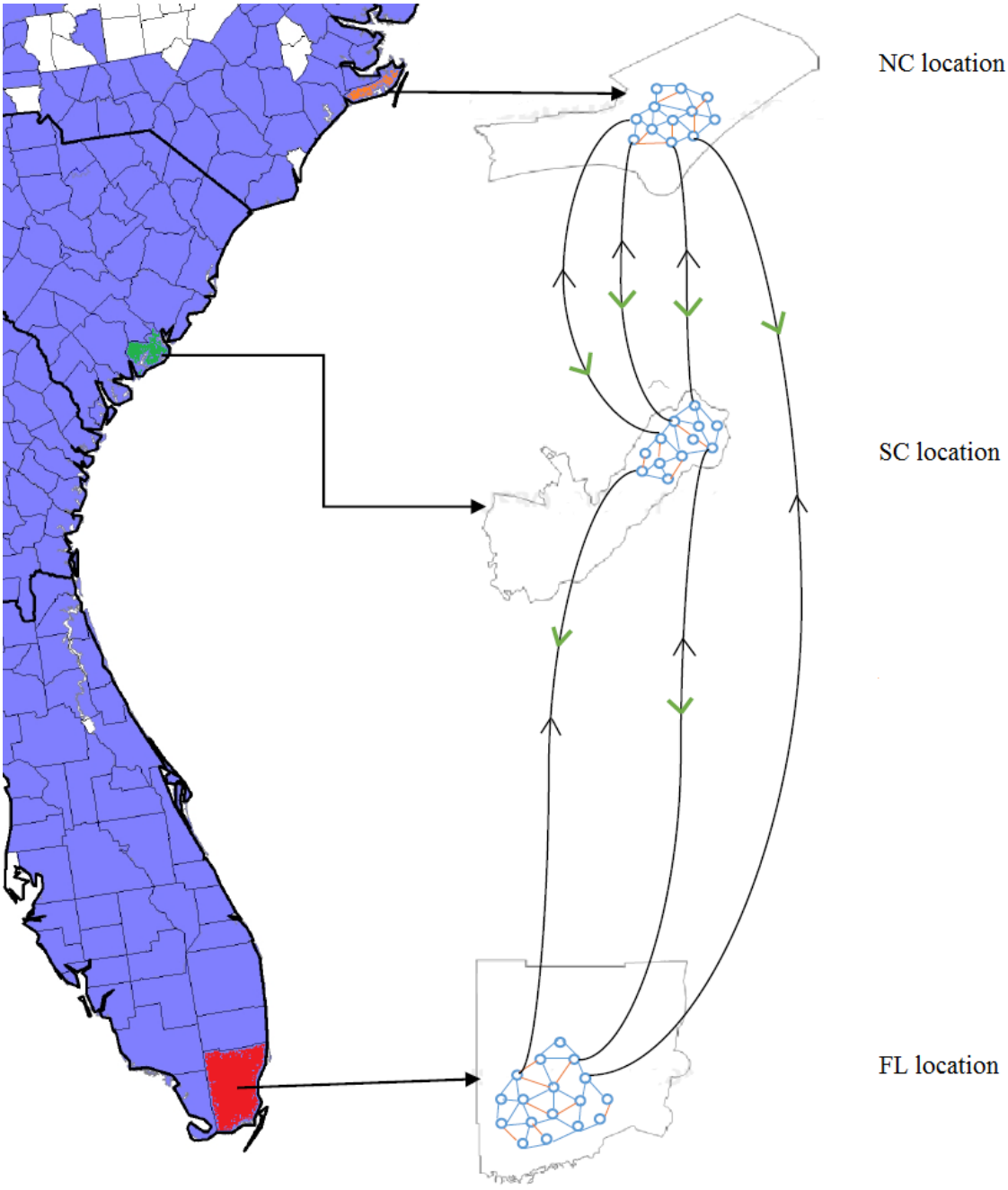


Figure 2.2: The network layout of three locations for JE spreading. Purple shades in the map indicate the presence of feral pigs [32]. Green arrows indicate directions of migration during fall migration period, and black arrows indicate the direction of migration during spring migration period. Blue circles represent feral pigs, blue lines represent direct links for possible transmission

of the JE virus via mosquitoes, and orange lines represent links for possible transmission via mosquitos and birds.

Table 2.1: Relative abundance of mosquito in FL, SC, and NC location during the different time period. A higher number of "+" sign indicates the higher abundance of mosquito.

Period	Month	Mosquito abundance		
		FL	SC	NC
Late summer	June-July	++++++	++++	+++
Early fall	August-September	++++++	+++	++
Spring migration	April-June	++++	++	+
Fall migration	July-September	++++++	++++	++

The long-distance pathogen transmission is unidirectional—northbound during spring migration between three locations and southbound during fall. The migration pattern in our network is shown in Figure 2.2 a-b.

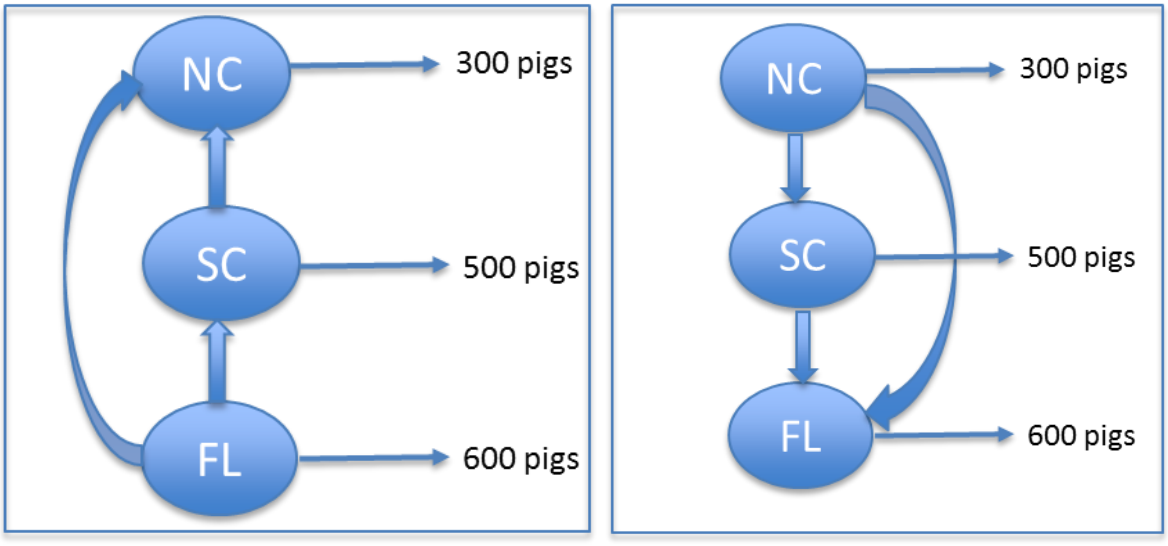


Figure 2.3: Simplified representation of our network with three spatially separated locations during (a) northbound spring migration period (b) southbound fall migration period. The tip of the arrows indicates the direction of bird migration. The blue ellipses represent the geographic locations. The numbers indicated beside each ellipsis are the numbers of feral pigs in that corresponding location.

Within each geographical location, resident birds, mosquitoes, and pigs can move randomly in any direction. Pathogen transfer is highly dependent on the migration pattern of birds as various species have distinctive intervals between the staging places (places where birds take a break while migrating) and unique flying speeds while migrating.

2.3 Estimations and Assumptions

Pig population data used for our simulations are derived from the feral pig mapping system [32] These published maps of the distribution and density of feral pigs throughout the United States allow us to determine the estimated number of feral pigs in various locations. We consider all three of our locations having a medium density of feral pigs—10 animals per sq mi [33]. Consequently, 600 pigs in FL (60 sq mi area), 500 pigs in SC (50 sq mi) and 300 pigs in NC (30 sq mi) are selected. Therefore, our model contains a total of 1400 pigs (nodes in the network) within the three locations. We start each simulation with a single infected pig in the initial location of the bird migration. Therefore, we assume one infected pig in FL and NC location respectively for spring and fall migration. Selection of other density (low, high) of pigs would change the population in each location. Therefore we would have results with similar trends but different quantitative values.

In our model, we use a complex weighting system, a crucial factor in our simulation model, as weights are used to reflect the heterogeneity in mosquito and bird populations in different

locations. Weights represent the temporal and spatial dependence of mosquito vectorial capacity β_1 in the different locations during fall and spring migrations. Mosquitoes are abundant in all three locations during fall migration, but the FL location always contains more mosquitoes than the other locations. Therefore, the selected weight ratio of FL: SC: NC during fall migration is 3:2:1 (values are 1.5 β_1, β_1, and 0.5 β_1 respectively) and 4:2:1 during spring migration (values are β_1, 0.5 β_1 and 0.25 β_1 respectively). We chose mosquito vectorial capacity values for our simulations in such a way that they remain within a realistic range after the weighting [34]. Weights ratios reflect the relative abundance of mosquito within each simulation period (fall and spring) while the value of weights represents the actual abundance of mosquito. An important point here— this is just one scenario chosen for simulation purpose in this model, it could have been chosen otherwise by reflecting the higher abundance of mosquito during fall than spring migration period. In our result section, we express all Figures only through β_1 and r; However, different values of β_1 in each location are considered following the weighting system, as parameters are weighted with corresponding weights of that location and season.

The bird community parameters in these locations are dependent on the number of available WNV- (Komar et al. 2003) and JE-competent birds at these locations. A list of WNV and JE competent birds are presented in Table 2.2 and Table 2.3, respectively.

Table 2.2: WNV-competent birds, their presence in selected locations, and migratory statuses from Komar et al. 2003 [24].

Name of birds	Presence	Migratory status
American coot	FL SC NC	Yes
American crow	FL SC NC	No

American kestrel	FL SC	No
American robin	FL SC NC	Yes
Black-billed magpie	FL	No
Blue jay	FL SC NC	No
Budgerigar	FL	No
Canada goose	FL SC	Yes
Common grackle	FL SC NC	Yes
European starling	FL SC NC	No
Fish crow	FL NC	No
Great horned owl	FL NC	No
House finch	NC	No
House sparrow	FL	No
Japanese quail	FL	No
Killdeer	SC	Yes
Mallard	FL SC NC	Yes
Monk parakeet	FL NC	No
Mourning dove	FL SC NC	Yes
Northern bobwhite	SC	No
Northern flicker	SC	Yes
Red-winged blackbird	FL NC	Yes
Ring-billed gull	FL SC NC	Yes
Ring-necked pheasant	FL	No

Table 2.3: Most prevalent JE-competent bird species in selected locations with migratory statuses

Name of birds	Presence	Migratory status
American bittern	FL SC NC	Yes
Black crowned night heron	FL NC	Yes
Cattle egret	FL SC NC	Yes
Great blue heron	FL SC NC	Yes
Great egret	Fl NC	Yes
Green heron	FL SC NC	Yes
Least bittern	FL SC NC	Yes
Little bLue heron	FL SC NC	Yes
Snowy egret	FL	Yes

The values of *r* for NC, SC, and FL are weighted for all simulations with 22/33, 20/33, and 29/33, respectively. This set of weights are derived from a list of WNV- and JE-competent birds of 33 total species and the availability of bird species from that list in the corresponding locations. For example, the FL location contains 29 bird species out of the 33 competent species, hence the weight 29/33.

The pathogen transfer rates β_3 via migratory birds are expressed with the vectorial capacity of two locations. The migration process being independent of the origin and destination locations, β_3 is expressed as the product of β_2 of two locations and weighted with the fraction of the number of migratory species for each location to the total number of species**.** Therefore, the weights for β_3 for FL, SC and NC are respectively 18/33, 14/33 and 15/33.

Chapter 3 - Simulation Results

We compared the total number of infected pigs for three different bird community parameters (r) and increasing values of mosquito vectorial capacity (β_1) during both the fall and spring migration period using two different network types.

Simulation results for a locally fully connected network and various bird community parameters (r = 0.15, 0.3, and 0.5) are presented in Figures 3.1-3.2.

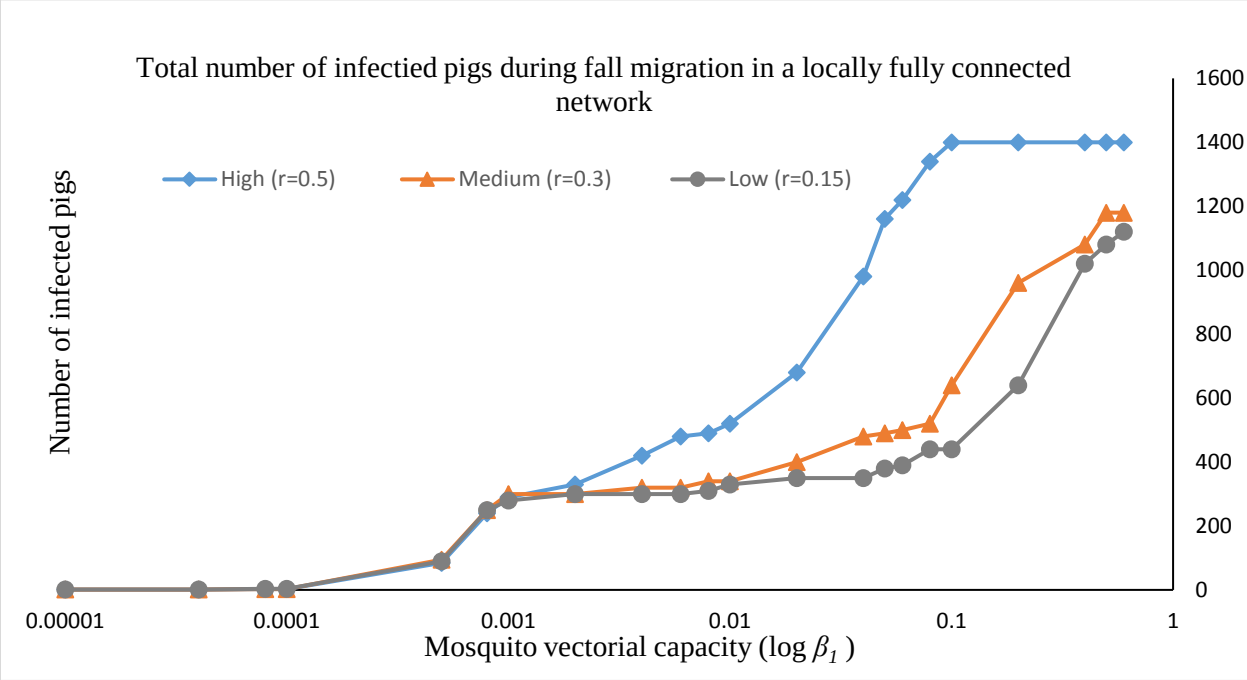


Figure 3.1: Estimated number of infected pigs during fall bird migration using a locally fully connected network. Japanese Encephalitis incidence in pigs increases with vectorial capacity. The number of infections remains similar for all bird community parameters until a vectorial capacity β_1 =0.001, after which high bird community parameter leads to significantly more infected pigs. For less diverse communities a plateau around 300 infections indicates that pathogen spreading is confined only within the initial location.

The simulation starts with a single infected pig in the NC location for fall migration. The infection spreading within a location did not start until vectorial capacity reached a value of 0.0001. For r=0.5, the number of infections reached its maximum at the vectorial capacity of 0.1. For other values of r, however, the number of infected nodes did not reach their maximum within our simulation period because the spread of the pathogen to distant locations was highly dependent on bird community parameters. We observed a region of slow growth rate in Figure 3.1 around the number of pigs (300 total infections) of the initial location, followed by a region where the number of infected reached at maximum very rapidly for high values of r.

Figure 3.1 shows that an increase of r caused the number of infections to reach its maximum value at a lower vectorial capacity compared with curves for low and medium r. This happens because in case of increased bird population, birds dispersed within a larger area in search of food. This spatial spread of birds provided spatially separated mosquito communities the opportunity to bite the same individual bird, making the pathogen transfer much faster. The number of infections at the end of the simulation period did not reach maximum (total number of infected individuals = 1400) for r = 0.15 and 0.3 because the rate of pathogen transfer was slow for lower bird community parameter. The number of infections in all cases were bounded to reach a maximum of 1400 if the simulation ran for infinite time, given that we assumed fixed population sizes and no recovery of the pigs.

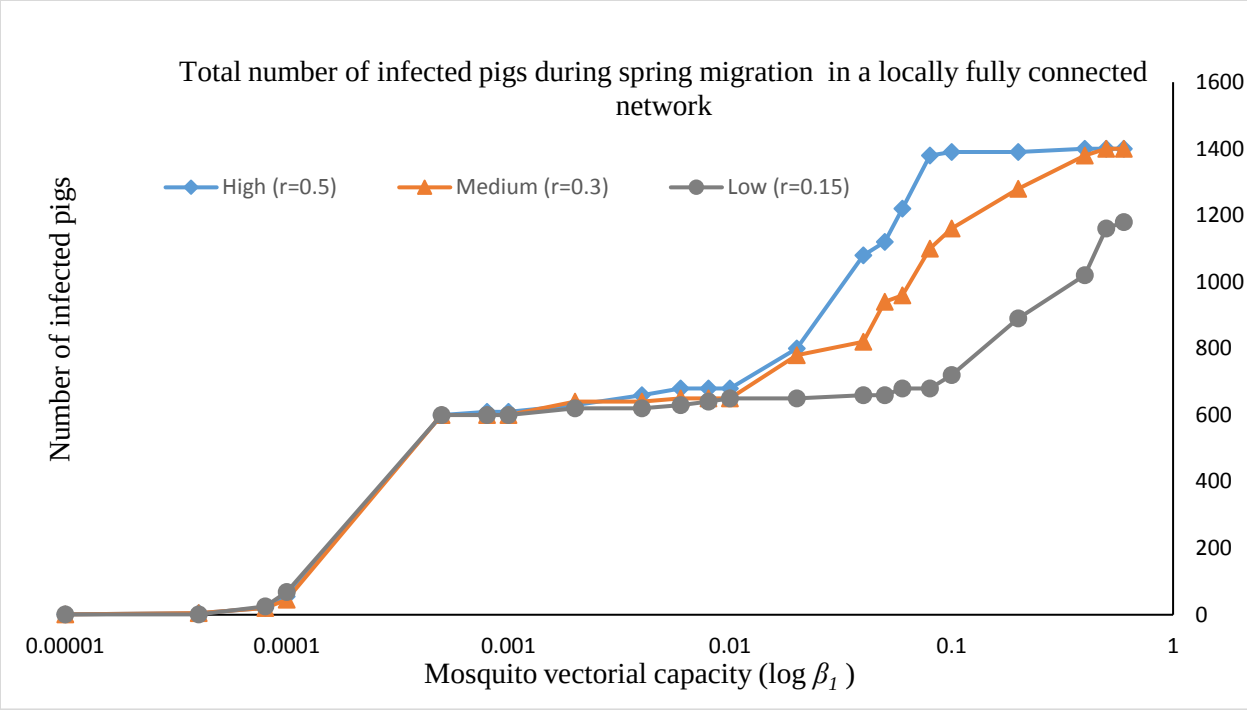
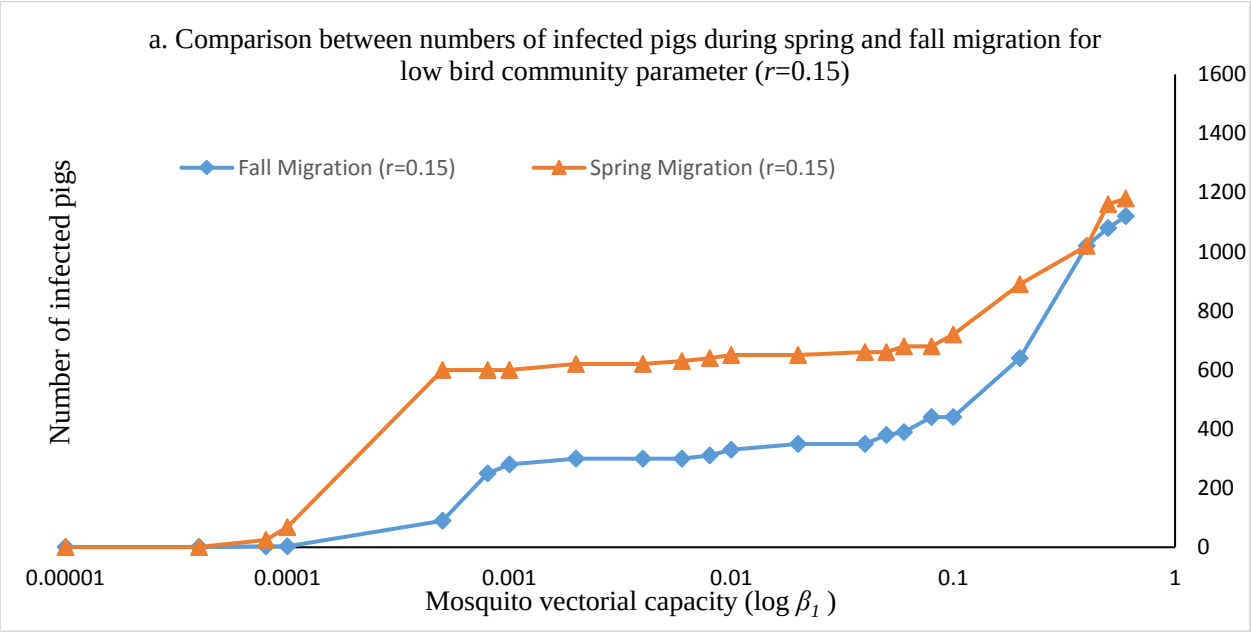
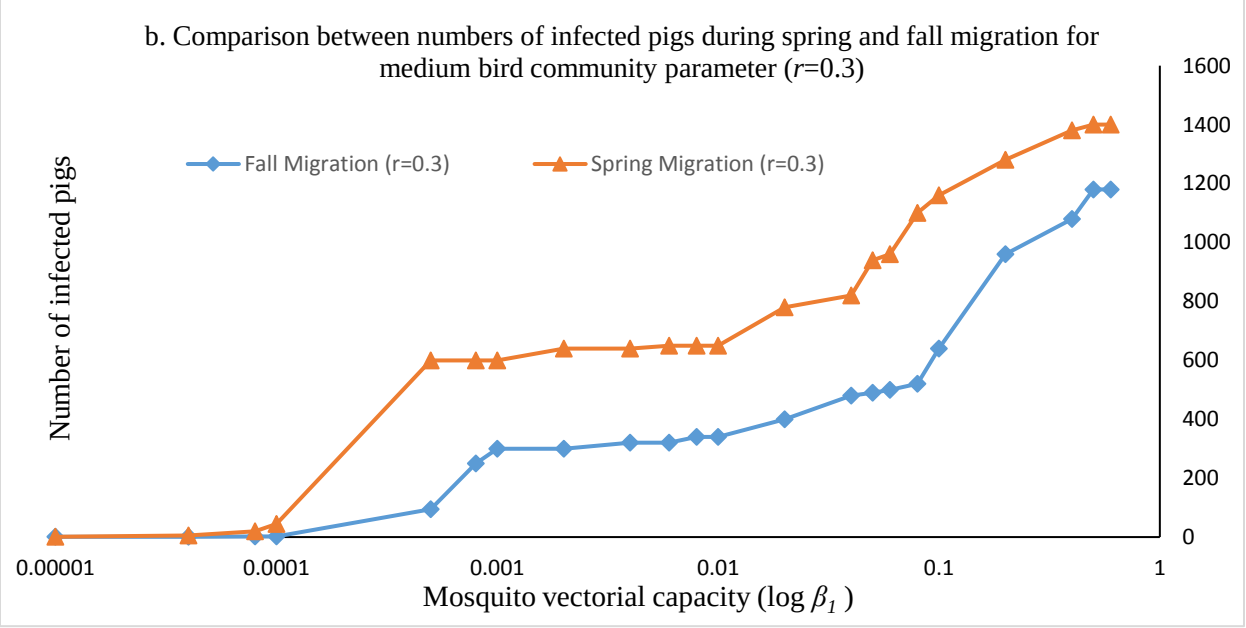


Figure 3.2: Estimated number of infected pigs during spring bird migration using a locally fully connected network. The number of infections remains almost similar up to a vectorial capacity of 0.01 for all bird community parameters. A plateau is pronounced around 600 infections after which the number of infections reached the maximum for high and medium bird community parameters.

We began our simulation for spring migration with one infected pig in the FL location, which consisted of a total of 600 pigs. The infection spreading began at a vectorial capacity of 0.00006 (Figure 3.2). The overall pattern of increasing numbers of infected pigs followed the same trend as fall migration. For both migration periods, the infection started increasing until reaching to the number of infections of the initial location, followed by a plateau. After the plateau, the number of infections again started growing. The plateau was for all bird community parameters during spring (Figure 3.2) while that was for only for medium and low bird community parameters during fall migration (Figure 3.1). The significant lower vectorial capacity in all locations during spring migration than fall was the main reason for this difference. Therefore, although birds from the

initial location were migrating, there weren't a sufficient mosquito population to initiate a transmission cycle in the second location, or migratory birds were never infected in the origin location at all.





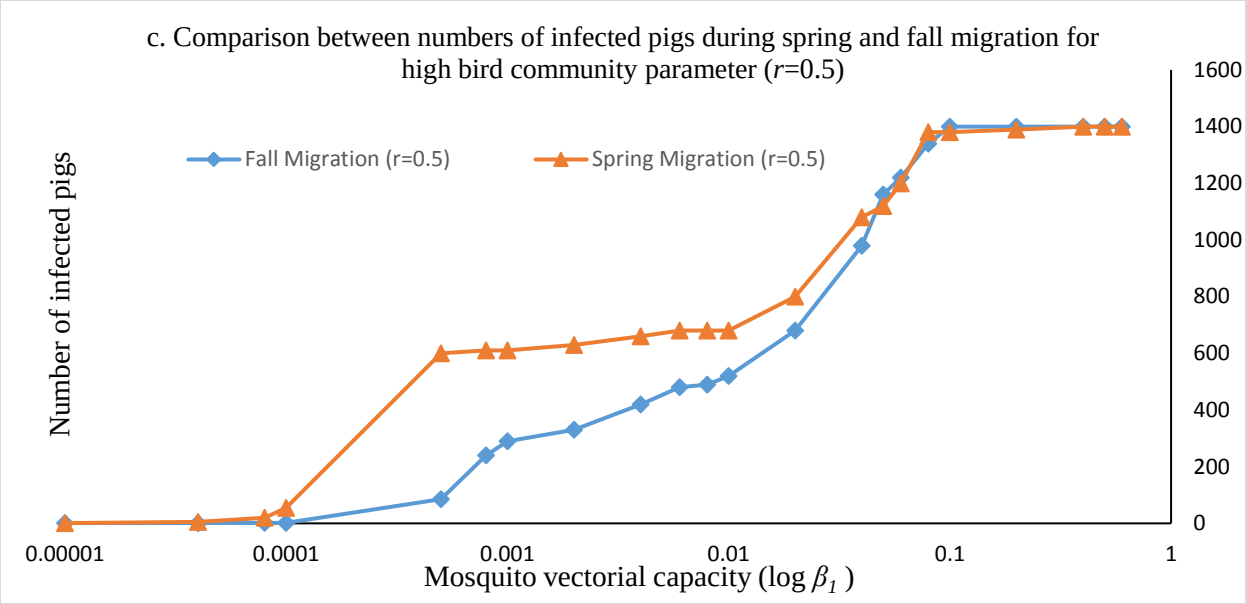


Figure 3.3: Comparison between the number of infections of the locally fully connected network during spring and fall migrations for increasing values of vectorial capacity when a) r = 0.15, b) r = 0.3, and c) r = 0.5. There are plateaus around the number of populations of the initial location for lower values of bird community parameter r for both migrations while there is no plateau during fall migration for high bird community parameter. For spring migration the infection reached the plateau at a lower value of vectorial capacity than fall.

Figures 3.3 a–c showed that the numbers of infected pigs were always greater or equal during spring than during fall migration. This was attributed to the introduction of infection in a region of high migratory and local bird community parameter and mosquito abundance. Figure 3.3 (a) shows that the infection did not reach the maximum value of 1400 because bird community parameter was much less which made the probability of pathogen transfer to a distant location limited. For high bird community parameter, infection reached the maximum around vectorial capacity of 0.1 for both migration periods because increased abundance of birds caused the infection to reach distant locations at a faster rate.

Same procedure as for the locally fully connected was applied for the locally Erdos-Renyi network model, and simulation results are presented in a similar fashion in the following.

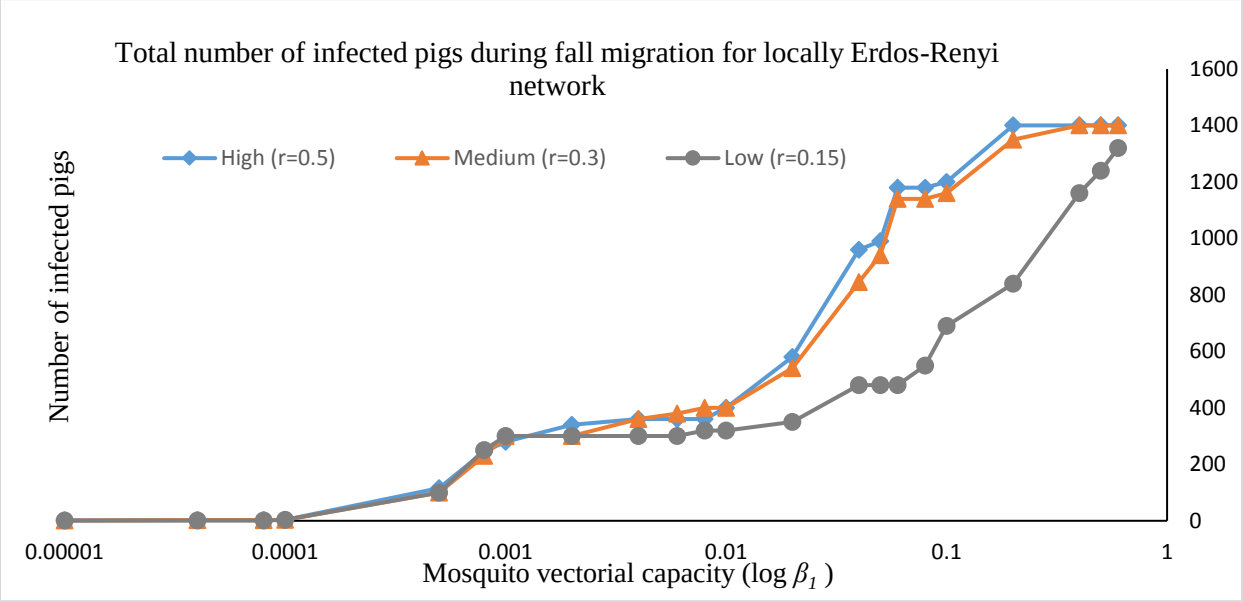


Figure 3.4: Estimated number of infected pigs during fall bird migration using a locally Erdos-Renyi network. Around 300 infected pigs, there is a plateau up to vectorial capacity 0.01 for all bird community parameters. The number of infections increases at almost at a similarly for high and medium bird community parameters after the plateau.

In Figures 3.4 and 3.5, an increasing pattern in the number of infections similar to the locally fully connected network was noticeable for fall and spring migration period respectively. The total number of infected pigs attempted to reach the full population size of the initial location. When the vectorial capacity reached at 0.01, numbers of infected pigs again started increasing faster until it reached the maximum for higher bird community parameters. If the vectorial capacity did not reach at 0.01, the rate β_3 (the transfer rate from one to location to another) remains too insignificant to start an infection at a distant location, as mosquito abundance in both locations was too small. However, when the vectorial capacity exceeded that point (vectorial capacity 0.01), the number of infections demonstrated a faster increase for high and medium bird community parameter.

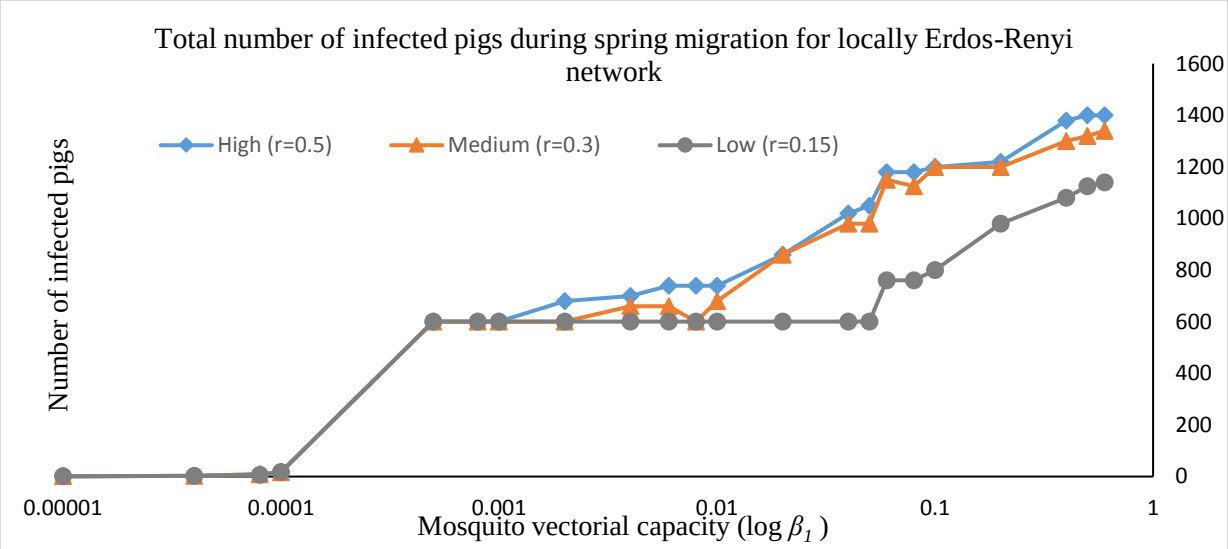
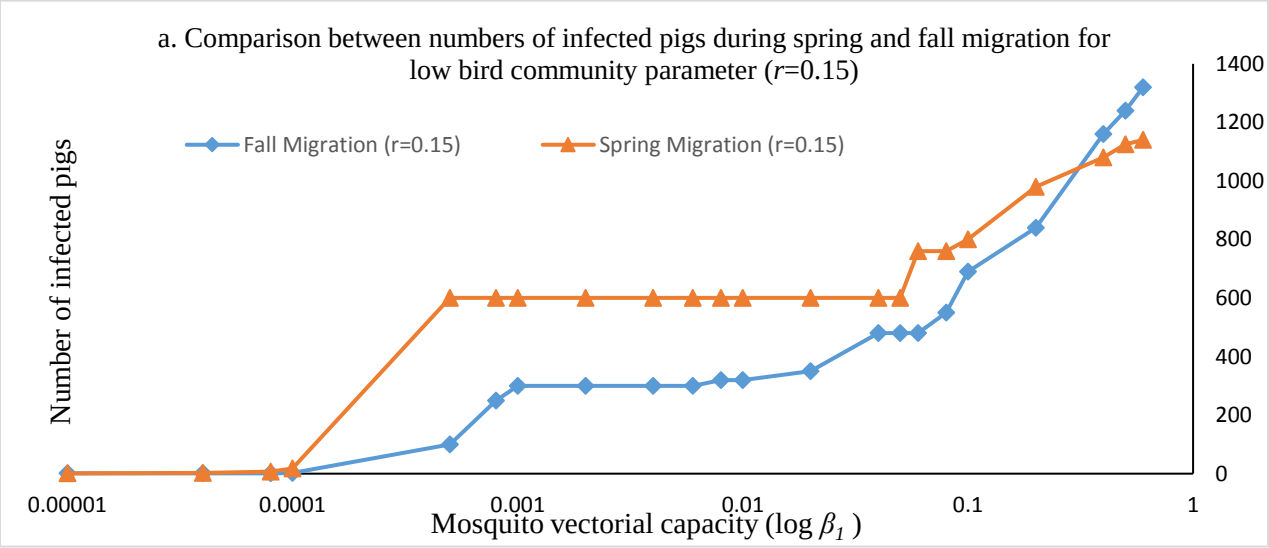
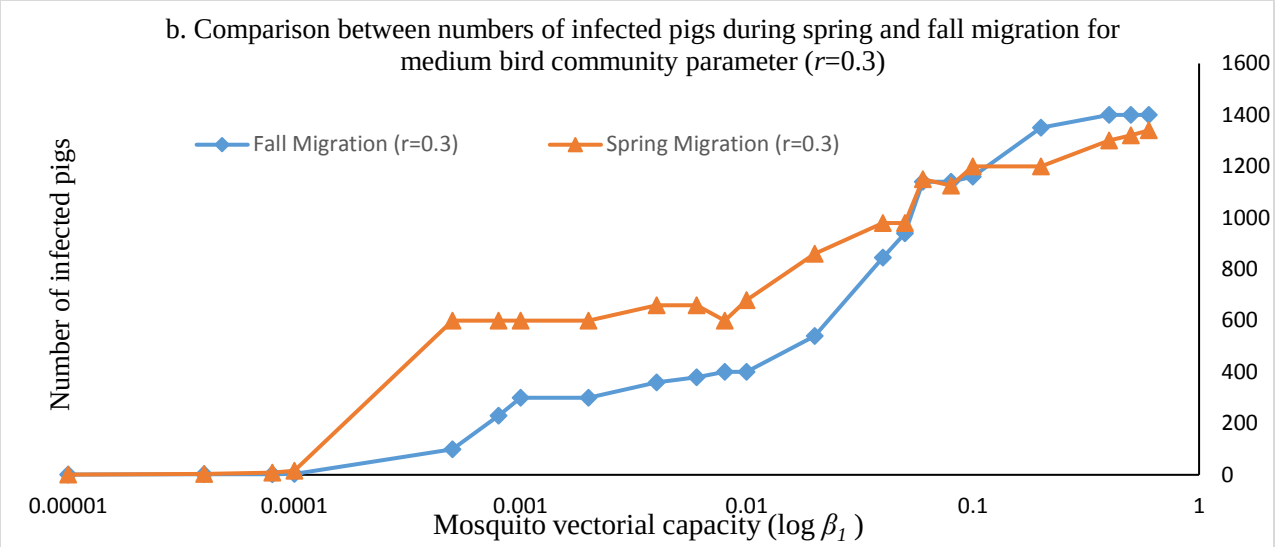


Figure 3.5: Estimated number of infected pigs during spring bird migration using a locally Erdos-Renyi network. Around 600 infected pigs, there is a plateau up to vectorial capacity 0.01. The number of infections increases at almost at a similar fashion for high and medium bird community parameter after the plateau.





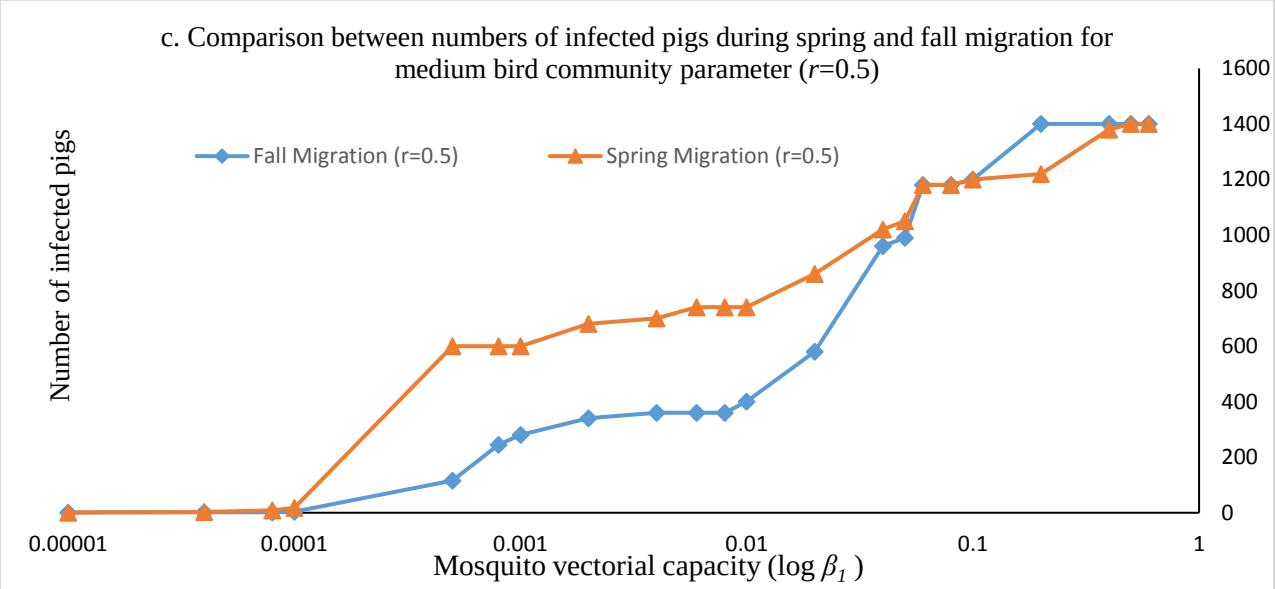


Figure 3.6: Comparison between the number of infections of locally Erdos-Renyi network during spring and fall migrations for increasing values of vectorial capacity when a) r = 0.15, b) r = 0.3, and c) r = 0.5. There are plateaus around the size of the population in the initial location for all bird community parameters during both migrations. For spring migration, the infection reached the plateau at a lower value of vectorial capacity than fall. The total number of infections during spring migration does not reach the maximum for medium and low bird community parameters while always reaches maximum for fall migration.

Figures 3.6 a-c showed plateaus in the number of infected individuals around the initial location population of 300 for fall migration and 600 for spring migration. Following the plateau for spring migration, numbers of infected individuals did not reach the maximum value due to the low mosquito density in the SC and NC locations. For fall migration, however, following the initial slow pathogen transfer in the NC location, the number of infected individuals increased rapidly to reach the maximum. This rapid increase was attributed to the high mosquito density in all three locations, specifically in the SC and FL locations.

Chapter 4 - Discussion

Computational models (mechanistic transmission models) are very important tools as they aid us in studying systems for which experimental studies are expensive or unethical. Success of these models is contingent upon proper estimates of these parameters. However, for the vast majority of systems and particularly for biological systems, we lack reliable information about parameters. Statistical models can be more accurate at predicting disease outbreaks in real time than other models for parameters being estimated from incidence data. However, statistical models can not suggest mitigation strategies. Therefore, to develop model in advance of any potential threat of an epidemic and to suggest mitigation strategies against a disease, mechanistic approaches constitute the best option for modeling.

In this report, we were focused on formulating a transmission model for JE in the USA and suggesting efficient mitigation strategies. However, JE incidence has not been reported in the USA. Therefore we choose mechanistic transmission modeling approach being a suitable model in the absence of incidence data. From Figures 3.1-3.6, it was evident that after the plateau, pathogen spread was an increasing quantity with bird community parameter. This demonstrated that the bird community parameter motivates an expeditious increase in the number of infected pigs. However, increase in the value of *r* cannot function to its full extent until a certain value of vectorial capacity (0.01) is reached, as we can see from Figures 3.1-3.6. Therefore, mosquito vectorial capacity is the primary factor, and bird density and diversity is the secondary factor for the spread of the JE pathogen.

Comparisons of the average number of infected pigs during fall and spring migrations for our two network models showed different trends. The average number of infections in the locally fully

connected network was greater during spring than fall migration for all bird community parameters, although they occasionally coincided at high and low values of vectorial capacity. In the Locally Erdos-Renyi network, however, the increase in the pathogen spreading was much faster during fall migration after initial plateau than spring migration. This contradiction is essential for determining the closeness of our model to reality.

As mentioned, JE has not been introduced to the United States, so incidence data of WNV was used to determine the model's ability to portray accurately real-life incidences. The incidence data of WNV shows that most of the cases occurred between May and October, peaking at the end of August to the beginning of September [31]. This period closely matches the migratory pattern of the birds. Spring migration typically occurs from April to June, while fall migration typically begins at the end of July and continues until October for some species. As the fall migration period coincides with peak occurrences of WNV incidences, fall migration was identified as an important factor in the pathogen spreading. Mosquitoes were also abundant in all locations during this period, leading to widespread infection. During fall migration period, a faster increase in the number of infections than spring as well as total infected cases for locally Erdos-Renyi network closely resembled the peak incidence period of WNV. Also, high mosquito abundance in all locations during fall migration period should result in a faster spreading in pathogen than spring migration, which was also demonstrated in the simulation results (Figures 3.4-3.6) obtained from locally Erdos-Renyi network. However, the locally fully connected network resulted otherwise creating more infections during spring than fall migration period. Therefore, among our two networks, the locally Erdos-Renyi one best described real-life scenario of the pathogen spreading. Therefore, locally Erdos-Renyi seems a better network model to be adapted to determine the spread of JE in the United States.

Simulations for locally Erdos-Renyi network in the Bronx County, NY, resulted in one infected human for maximum vectorial capacity value (0.6) used and high bird community parameter (r=0.5). Therefore, we increased the vectorial capacity further and for a highest physical value of 1.54 [34], number of infected cases reached up to three. Our simulation results (1-3 human cases) encompassed the average number of WNV cases (2.38 human cases) in the NY locations since 2003 [31]. For medium and low bird community parameters, simulation results showed no human cases, because reduced bird abundance made the transmission of pathogen much harder. Therefore, high mosquito abundance was required along with a high bird's density to transmit the pathogen to human.

Our simulation results showed if values of vectorial capacity were less than 0.01, then the number of infections were almost independent of the value of r since all values of r resulted in an identical number of infections. Vectorial capacities greater than 0.01 caused a rapid increase in the number of infections in connection with increased values of r. Mitigation strategies for an incidence of JE in the USA can be effectively deduced from this trend. If mosquito vectorial capacity is less than 0.01, then insecticidal spray further reduce the mosquito population and the infection does not spread much and is contained within a small area (area of initial infection). For higher values of β_1 (more than 0.01), the number of infected is very sensitive to mosquito and birds as seen from simulation results. Therefore the highest priority at that time should be to control the birds as well as mosquito in that location to stop the distant spreading. Now from the plateaus we see that, within that region, reducing the mosquito density or bird density has no affect. This happens as all the feral pigs are infected at that time in the introductory location of the epidemic and infected pigs don't recover once infected. Therefore, unless infected pigs are removed from there, they continue to infect susceptible mosquitoes and birds in that location. Birds can be controlled by spraying the

area around the bird nests or rookeries. This would reduce the incidence of mosquitoes and the bird infections. Another option is to vaccinate birds for the pathogens so they do not get sick. There are also other novel methods that can be used to reduce bird exposure to mosquitoes. Culling of birds should be used as an option of last resort.

Chapter 5 - Conclusions

Our individual-level network model of JE has three compartments and three parameters. Weights assumed for bird community parameter can be deduced accurately if specific bird and mosquito abundance data were available. Given that we have these data about birds and mosquito, our approach reduces numbers of compartments and parameters that were used in earlier JE models.

Our model is flexible to the inclusion of heterogeneity in the contact structure among feral pigs as well as the host preference of mosquito. Meta-population and deterministic models are not capable of reflecting the heterogeneity in model populations. The scarcity of information about reservoir and vector population compelled us to use random network structure in this report. However, our model is a novel approach in modeling JE when specific population contact data is available.

For the local Erdos-Renyi network, although the infection starts at NC with fewer pigs (300 pigs) in fall than spring migration (600 pigs), the total number of infections increases much faster than spring migration for all bird diversities. From the data of human WNV incidence, the total number of infected peaks during fall migration period As well. The local Erdos-Renyi network simulation results in a maximum number of infected pigs at a time period similar to maximal WNV incidence for the specific geographic locations. Therefore, it can be deduced that Local Erdos-Renyi network better describes the epidemiology of JE in the USA.

This report also investigated effective mitigation strategies against JE and found insecticidal spraying can limit the infection within a geographical area of low mosquito vectorial capacity. For high values of vectorial capacity, control of birds from the infected area is required to reduce the spreading of JE to distant locations. These strategies can be applied to stop human infections from occurring in the scenario of JE spreading in the NY location. If the mosquito vectorial capacity is

high in the NY location, then removal/control of birds will necessarily prevent human infections according to the models.

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