Understanding the effects of the direct contacts and the indirect contacts on the epidemic spreading among beef cattle farms in southwest Kansas

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Abstract

Moving infected animals and sharing contaminated equipment and vehicles are considered as the most effective ways for between-farm disease transmission. The objective of this study is to develop a network-based simulation model to investigate the effects of direct contact, indirect contact, and their combination on a hypothetical foot-and-mouth disease spread between beef-cattle farms in southwest Kansas, the US. Based on synthetic cattle and truck movement data in southwest Kansas, we build a farm-level contact network with two layers, a cattle movement layer (direct contacts) and a truck movement layer (indirect contacts). The S-E-I-R model is selected to describe the epidemiology of the foot-and-mouth disease with some parameters adopted from published literature. For two parameters — detection time and indirect transmission rate — we perform a sensitivity analysis. Through a thorough simulation analysis of three sets of scenarios, we compare the disease transmission dynamics, the distribution of outbreak epidemic size, and the disease breakout percentage — note that for some simulations an initial infection will not produce a disease outbreak — of different contact structures. Simulation results show that neither direct contact nor indirect contact individually can result in a massive outbreak of the disease, but their combination plays a significant role. Additionally, we detect different probabilities of disease outbreak by starting the simulations at different farms; starting at some farms with high node strength increases the probability of disease outbreak. However, the immunization of the high-risk farms is not enough to control the disease spreading. What's more, we find that the detection time and indirect transmission rate have great impacts on the epidemic size and disease breakout percentage.

Introduction

Foot-and-mouth disease (FMD) as a highly contagious disease that can lead to destructive economic losses in vast geography has been extensively studied in the past decades. Several major outbreaks have occurred in recent years in previously FMD-free countries, including the UK, Netherlands, France, South Korea, Japan, Uganda [1–4]. FMD spreads through "direct contact" [5,6], either among cattle in proximity or over long distances via cattle movements. On the other hand, FMD can be transmitted between cattle premises through fomites such as personnel, vehicles and agriculture tools, i.e., "indirect contacts," and have gained people's attention especially after the 2001 FMD outbreak in the U.K [7–10].

Accounting for \$78.2 billion in cash receipts in 2015, the beef industry is an important sector in the U.S. economy. FMD outbreaks once occurred would result in devastating consequences to the country's economy. Several studies have modeled the hypothetic FMD outbreak in the U.S. to estimate the potential economic loss. Pendell et al. estimated the financial loss of an outbreak constrained to Kansas would vary from \$43 to \$706 million determined by the livestock species initially infected [11]. Schroeder et al. reported a loss of as many as 7,000-8,000 livestock herds and 16-18 million animals for a regional, central U.S. outbreak [12]. Pendell et al. estimated a loss of around \$16–140 billion for an outbreak in the Midwestern U.S. originating from the proposed National Bio and Agri-Defense Facility in Kansas [13].

Liu et al. [6] presented a spatially explicit agent-based simulator for synthesizing beef cattle movements, and provided insight into the influence of network dynamics on epidemic dynamics. It was shown that the new infections were driven by the trading behavior, and that the removing rate determined whether the virus could survive long enough to infect others. Thakur et al. [14] developed an agent-based, stochastic, farm-level, state transition computer simulation model with the incorporation of network-structure among the swine farms for the between farm spread of porcine reproductive and respiratory syndrome (PRRS) virus to assess the impact of contact structures on between-farm transmission of PRRS virus. It was shown that scenarios considering only direct contacts resulted in lower overall epidemic sizes than that for scenarios in which both direct contact and indirect contact network were considered. Besides, epidemic size under scale free network was greater than that under the random or small-world network. Based on the data on veterinarian on-farm visits in a dairy farm system, a simulation model was built to assess the role of indirect contacts on epidemic dynamics compared to cattle movements (i.e. direct contacts) [15]. Rossi et al. [7] obtained a threshold for $\beta_{ind} = 0.25$ and concluded that indirect contact had a larger impact on disease transmission compared to direct contact network.

Yang et al. [16] built an agent-based model to simulate the FMD transmission through truck and cattle movement following an independent clean-infected-clean cycle. The results showed that including indirect contact routes between premises via truck movements could significantly increase the amplitude of disease spread compared with equivalent scenarios that only consider animal movement. For example, the median number of infected producers changed from 4 to 82 in the producer isolation scenario, which could be taken as the equivalent one used in this paper.

In this paper, we take the beef cattle industry in southwest Kansas (SW KS) as a case study. Ranking third in the U.S., Kansas' cattle on feed reached 2,450,000 head by January 31, 2018. The beef cattle ranching and farming sector is the largest part in Kansas agriculture industry, with 42,228.4 employees and it contributes approximately \$8.9 billion to the Kansas economy.

Understanding FMD spread dynamics is of great necessity to implement appropriate mitigation strategies, e.g., movement restriction, culling animals on detected farms, enhancing the cattle production resilience. In this study, we use the synthetic cattle movement data generated in Yang et al. [17] to build a direct contact network and indirect contact network. Our goal is to present insights into the effects of direct and indirect contacts on the epidemic spreading among 301 beef cattle farms in southwest Kansas, US. First, we generate a farm-level, weekly-resolution temporal network of direct and indirect contacts. Then, a disease spread simulation model is developed using the Generalized Epidemic Modelling Framework (GEMF) [18]. Under three different scenarios, extensive simulations are carried out to test which type of contact structures has more impact on FMD spreading and how to develop better strategies to protect livestock from infectious diseases.

Materials and Methods

Beef-cattle farms and movement data

In this study, a two-layer contact network is generated based on the synthetic data from Yang [19] where the cattle trading records and cattle transportation information (like the truck identifier, origin farm identifier, destination farm identifier, headcount of cattle carried by truck and transport date) among 18 ranches, 50 stockers, 233 feedlots, 4 packers and 12 entry points in SW KS are simulated using an agent-based model. Focusing on a hypothetical FMD outbreak among farms inside SW KS, we ignore the entry points and packers because cattle transported through entry points are coming from outside of this region and the packers are endpoints.

Since cattle movements from ranches to stockers in SW KS mainly occur in the second half of the year, we use data for the last 26 weeks. To capture the dynamic characteristics of the contact network, weekly snapshot dynamic two-layer networks are considered in this study. Static networks generated weekly are switched with the simulation calendar. In the first layer, the cattle movements are represented as directed weighted links with weights equal to the average number of cattle transported between farms per day in a week. In the second layer, similarly, undirected weighted links represent the average number of trucks commuting between two farms per day in a week.

Individual-based epidemic model

To simulate the disease spread between beef-cattle farms, we develop a farm-level, stochastic, individual-based epidemic model on GEMF. GEMF can numerically simulate any stochastic GEMF-based model and is available in MATLAB, R, Python, and C programming language. It has been widely used to simulate spreading processes on multilayer networks. In this work, we further adapt GEMF in Matlab for simulations incorporating weekly snapshot of two-layer dynamic network.

In this paper, we adopt the susceptible-exposed-infectious-removed (SEIR) model to describe the epidemiology of FMD , as presented in Fig 1. In this model, there are four compartments, namely susceptible (S), exposed (E), infectious (I), and removed (R) four compartments, and each farm is categorized in one of them. The susceptible (S) compartment denotes the farms where all cattle are unexposed to the pathogen and can be infected by the interactions with infectious (I) farms. Once any of the cattle become infected, the farm will be categorized as exposed (E) in the first few days and then transit to infectious (I). Exposed (E) is a stage where the farms are infected but not yet infectious. Infectious farms become removed (R) when they stop all interactions with other farms. The transitions happening spontaneously are defined as the nodal-based transitions (E to I and I to R). The other type of transitions are edge-based, for example, the transition from S to E. A susceptible farm becomes exposed only if it has connections with other infectious farms. We assume that the infection process of a farm with one infectious neighbor is a Poisson process with transition rate β and that the processes are stochastically independent. Therefore, for a susceptible node with more than one infectious neighbors, the transition rate is the infection rate β times the number of infectious neighbors. The neighborhood of each node is determined by a contact network. Therefore, the transition rate from S to E is $\beta_{dir}Y_i + \beta_{ind}Y_i$ in our case. Exposed farms transit to infectious state with rate λ. Finally, infectious farms are removed with rate δ.

The parameters used in this model are specified as follow: infectious rate for direct contact $\beta_{dir} = 0.95 day^{-1} calf^{-1}$ [20], $\lambda = 1/3.59 day^{-1}$ [21] which means that the average incubation time is 3.59 days. For the infection rate of indirect contact β_{ind}, we use $\beta_{ind} = 0.1 day^{-1} calf^{-1}$ for the base scenario, since no specific value is available in

the literature. As the removing rate δ is strongly related to the mitigation strategy, we use $\delta = 1/14 day^{-1}$ [22] for the base scenario , which means that the average time for infectious farms becoming removed is equal to 14 days.

In the network presentation, each node represents a farm, each link represents a movement contact between farms. In Fig 1, the pair of nodes linked by a red dashed line are the same farm in two different network layers. The directed links on the cattle movement layer indicate that the disease can spread along that direction, while the links on the truck movement layer are undirected. Considering that the trade flow between different types of farms is unidirectional, for example, ranches sell calves to stockers but do not buy cows from other farms, the disease only spread along with the trade flow. Therefore, it is safe to conclude that the network of cattle movement is directed. On the other hand, because the truck movement is a round trip, the truck movement network is undirected.

Fig 1. Conceptual epidemic model that consists of a node transition graph and contact networks. Circles in the node transition graph represent the four compartments–susceptible (S), exposed (E), infectious (I), and removed (R). The arrows between the compartments show the direction of transition with rates β_{dir}(infection rate of direct contact), β_{ind}(infection rate of indirect contact), λ(incubation transition rate) and δ(removing rate). Nodes in the two-layer network represent individual farms, and red dash lines link the same nodes in two different layers. In cattle movement network, directed links indicate FMD transmission through cattle movement, i.e., direct contact. The undirected links in truck movement layer represent the transmission routes by fomites between premises, i.e., indirect contact.

For SEIR model, GEMF gives the individual-level Markov process for node i as Eq 1

$$
\begin{aligned}
P[x_i(t + \Delta t) = 2 \mid x_i(t) = 1] &= \beta_{dir} Y_i^1 \Delta t + \beta_{ind} Y_i^2 \Delta t + o(\Delta t) \\
P[x_i(t + \Delta t) = 3 \mid x_i(t) = 2] &= \lambda \Delta t + o(\Delta t) \\
P[x_i(t + \Delta t) = 4 \mid x_i(t) = 3] &= \delta \Delta t + o(\Delta t)
\end{aligned}
\tag{1}
$$

where $x_i = 1,2,3$ and 4 correspond to the susceptible, exposed, infectious or removed state of node i respectively. The value $X(t)$ is the joint state of all nodes-the network state at time t.

Scenario Analysis

To evaluate the potential risk of FMD spread in the two-layer contact network, we designed 3 sets of scenarios and 500 iterations of each scenario are simulated for 26 weeks during the second half of the year.

First, the transmission of the FMD virus by direct contact only, indirect contact only and combination of direct and indirect contact are simulated. The FMD virus is seeded in a randomly selected ranch, which is the head of the supply chain, in a randomly selected week of the first month. Parameters for base scenario are used here.

Additionally, based on the number of cattle traded by each farm, we select the one with the highest trade volume in each production type as the high-risk farm. Then, we initialize the disease one time from the high-risk farm and the other time from one randomly selected farm in the same production type. The two-layer contact network with the combination of direct and indirect contact is used in these scenarios. The features of the disease spread are compared. Also here, we used the parameters for the base scenario.

Lastly, a sensitivity analysis for two key parameters– the infection rate of indirect contact β_{ind} and the removing rate δ is performed for the contact network with 2 layers

by varying β_{ind} and δ individually. The infection rate of indirect contact β_{ind} ranges from 0.01 to 0.20 with 0.01 step. The reciprocal of removing rate, $1/\delta$ that reflects the infection duration ranges from 4 days to 23 days.

The outcomes of each simulation are the total number of the farms in each disease compartment over the simulation time. If there are at least 3 farms (1% of the total number of farms) infected at the end of the simulation time, we consider the disease breaks out, otherwise, the disease dies out. From the outcomes, we extracted the following measurements: 1) disease transmission dynamics, defined as the average fraction of farms in each compartment over time; 2) disease outbreak percentage, defined as the percentage of total simulations where the disease breaks out; 3) outbreak epidemic size, defined as the percentage of removed farms in iterations where the disease breaks out.

Results and Discussion

Effect of contact structures

The results of the average epidemic size over simulation time and distribution of outbreak epidemic size for different contact structures are presented in Fig 2.

Fig 2. Disease transmission dynamics and distribution of outbreak epidemic size for direct-contact-only network, indirect-contact-only network and the combination of direct and indirect contact network. Plots except the lower right one show the disease transmission dynamics after introducing the FMD virus to a random ranch. The direct contact scenario (top left): compartment R reaches the steady state 0.092 at 60th day; the indirect contact scenario (top right): the disease can hardly spread; direct & indirect contact scenario (bottom left): compartment R arrives steady state 0.401 at around the 100th day. Plot at bottom right reflects the simulation results where disease spreads at least to 3 farms. For direct contact only network, the median of outbreak epidemic size is 0.093; for indirect only contact network, outbreak epidemic size in most cases is less than 0.1. As for direct and inderect contact network (D&ID), the median of outbreak epidemic size is 0.632 which is much larger than the scenario with only one contact layer.

The disease outbreak percentages of these scenario are 67% (335/500) for direct contact only network, 19.4% (97/500) for indirect contact only network, and 71.2% (356/500) for direct and indirect contact network.

Comparing the results from Fig 2, we find that the disease can hardly spread through a single contact network. However, when we combine these two layers, we see huge growth in the epidemic size and endemic duration. In this study, the direct contact network is a directed network without loops, which prevent the reverse transmission of the disease. Even though the indirect network is undirected, the infectious rate for this layer is quite small, which prohibits the disease spread. However, the network with direct and indirect contacts combines the contributions of the two transmission mechanisms to the spreading, and generates disease outbreaks.

Effect of production type and high-risk farms

Node strength is defined as the total number of cattle traded through a farm in the last 26 weeks of the year. Fig 3 shows the distribution of node strength by farm types.

The distributions for these cattle producers indicates there are a small number of farms (hubs) having more frequent trade activities with other farms. The farms with

Fig 3. Node strength of the farms. Plots are the node strength of ranches, stockers and feedlots individually from top left to the bottom left

the highest strength in each type are the 129th farm that is a ranch, the 95th farm that is s stocker and the 120th farm that is a feedlot. The following scenarios are designed to explore the effect of these hubs on disease spread.

First, we initialize the disease from the high-risk ranch (the 129th farm) at a random week in the first month. From the top left panel in Fig 4, the steady state of compartment R is larger than the case with an initial random selected ranch infected shown in Fig 2, which means that the overall risk is higher if the high-risk ranch is initially infected. There are 483 over 500 iterations where the disease breaks out when the FMD virus is seeded in the high-risk ranch. Namely, if the ranch is initially infected, there is more than 90% probability that the disease will spread and produce an outbreak. However, the probability of disease outbreak when the virus is seeded in a randomly selected ranch is around 70% (356/500). Under the condition that the disease spreads, the distribution of outbreak epidemic size for both scenarios are quite similar, as shown in the bottom left panel of Fig 4. Therefore, if the disease starts from high-risk ranch, there is a higher probability that the disease will break out, but the outbreak epidemic size would hardly be influenced.

Then, we immunize the high-risk farms which are farms with index 129, 95 and 120, and start the disease from a randomly selected ranch different from farm 129. In this case, the steady state of compartment R is slightly smaller than the one in the case where those farms are not immunized, see the top right panel of Fig 4. The number of simulations with disease outbreak is 332, which is again slightly smaller. What's more, there is only a slight difference among the distributions of the outbreak epidemic size. The results show that the strategy which immunizes the farms with the highest strength is not effective for preventing the disease spreading when the disease starts from ranches.

Fig 4. Disease transmission dynamics and distribution of epidemic size when the high-risk ranch is initially infected and high-risk farms are initially immunized. Disease transmission dynamics when the high-risk ranch is initially infected (top left): compartment states reach steady state at around 100th day, and the steady state of R is 0.559; disease transmission dynamics when the high-risk farms are immunized (top right): states reach steady state at around 100th days, and the steady state of R is 0.355; distribution of outbreak epidemic size of FMD outbreaks (bottom one): the median of outbreak epidemic sizes for the cases where random ranch is infected, high-risk ranch is infected and high-risk farms are immunized are 0.632, 0.628, 0.584

We perform similar simulations for the high-risk stocker (the 95th farm), and report the results in Fig 5. First, a randomly selected stocker is initially infected at a random week in the first month. Then, we initialize the disease from the high-risk stocker at a random week in the first month. At last, we immunized the high-risk farms and started the disease from a randomly selected stocker different froom the high-risk stocker.

Among 500 simulations for each scenario, there are 187 simulations where the disease breaks out when a randomly selected stocker is infected; 271 disease outbreak simulations when the high-risk stocker is infected; and 162 disease outbreak ones when the high-risk farms are immunized.

The results in Fig 5 show that if the disease is initialized from the high-risk stocker, the probability for disease outbreak is higher than that in the case where disease starts from a randomly selected stocker, and that immunization of farms with high node strength is not enough for disease prevention. The disease transmission network is quite

Fig 5. Disease transmission dynamics and distribution of outbreak epidemic size when a randomly selected stocker and high-risk stocker is initially infected respectively and when high-risk farms are immunized. Disease transmission dynamics when a random stocker is initially infected (top left): the steady state of R is 0.179; disease transmission dynamics when the high-risk stocker is initially infected (top right): the steady state of R is 0.201; Disease transmission dynamics when high-risk farms are immunized (bottom left): the steady state of R is 0.144; distribution of outbreak epidemic size (bottom right): the medians of the outbreak epidemic size for the cases where a random stocker is infected, the high-risk farm is infected and high-risk farms are immunized are 0.601, 0.568 and 0.573

robust to targeted failures.

Comparing the results in Fig 4 and Fig 5, we notice that the difference between the disease outbreak percentage is large. Disease starting from ranches has a higher probability to spread. Furthermore, disease initialized from a ranch has a more concentrated distribution and greater value of outbreak epidemic size than the case where the disease starts from a stocker. The main reason for these is that ranches can reach more farms in direct contact network than stockers. Therefore, the risk of an outbreak when initializing the disease from a ranch is greater than that when stearting from a stocker.

When initializing the disease from a randomly selected feedlot, the disease cannot spread,since feedlot cannot reach any other farms in the direct contact network.

Sensitivity analysis on removing rate δ and indirect transmission rate β_{ind}.

We conduct a sensitivity analysis through a two-part approach. In the first part, we study the effect of the removing rate on FMD transmission. The reciprocal of the removing rate indicates the time needed by the regional administration to take actions from the day when the first case of the disease is detected. Therefore, how to choose this parameter is of great importance for disease control. We vary the removing rate δ from 1/4 to 1/23 while keeping other parameters in the base scenario unchanged. We perform 500 simulations for each δ. The fraction of infected farms over the total number of farms in southwest Kansas is recorded for each value of δ. The outbreak epidemic size distribution and the outbreak percentage are shown in Fig 6.

Fig 6. distribution of outbreak epidemic size and disease outbreak percentage when $1/\delta$ varies. Distribution of outbreak epidemic size (left); disease outbreak percentage (right)

The left panel of Fig 6 shows that the outbreak epidemic size increases when the removing rate δ decreases. The median of the outbreak epidemic size is fitted by polynomial in MATLAB. The trend could be obtained with Eq 2.

$$x = 129.36y^3 - 115.13y^2 + 39.19y + 2.87 \qquad (2)$$

where x denotes $1/\delta$ and y denotes median epidemic size. The time at which the epidemic size grow the fastest is at around the 8th day.

The right panel of Fig 6 shows the outbreak percentages for varying $1/\delta$. The variation of the set of data is 0.358. We calculate the linear correlation coefficient by Eq 3

$$r(X,Y) = \frac{Cov(X,Y)}{\sqrt{Var[X]Var[Y]}} \qquad (3)$$

The linear correlation coefficient of outbreak percentage and $1/\delta$ is 0.978, indicating that the number of days to farm removal is strongly correlated with the probability of disease outbreak.

In the second part, the effect of changes in the indirect contact rate on disease transmission is studied. The indirect contact rate reflects the ability of the disease vector to spread pathogenic bacteria. Adjusting the value of this parameter is equivalent to taking certain measures, such as cleaning and disinfecting vehicles. In this set of simulations, we have selected 20 different indirect contact rates β_{ind} ranging from 0.01 to 0.20 while keeping other parameters in the base scenario unchanged. Simulations results are presented in Fig 7.

Fig 7. distribution of epidemic size and die-out percentage when β_{ind} varies. Distribution of epidemic size of FMD outbreaks (left); Die-out percentage (right)

As shown in the left panel of Fig 7, the median of the outbreak epidemic size increases very quickly when β_{ind} is below 0.07. However when $\beta_{ind} > 0.07$, there is little difference in the median of the outbreak epidemic size. Therefore, we can conclude that controlling the infection rate of indirect contact β_{ind} can significantly reduce the overall number of infected farms. In practice, farms can clean their vehicles more frequently to reduce the value of β_{ind}. In addition, it is obvious that the outbreak epidemic size has a saturation effect on the parameter β_{ind}. In other words, the outbreak epidemic size (median and quartiles) changes slightly with the increase of β_{ind} once it reaches a certain value 0.06. When β_{ind} is between 0.01 and 0.06, the epidemic size grows rapidly. Once β_{ind} is above 0.06, the epidemic size reaches the peak, with the median value at around 0.63. However, from Fig 6, the median epidemic size can reach 0.75, suggesting that the removal rate limits the further increase.

In the right plot of Fig 7, the distribution of data points is more scattered and the variance of the outbreak percentage is 0.076 which is much smaller than the one for the removing rate. Besides, the correlation coefficient between the outbreak percentage and β_{ind} is 0.716, smaller than that of the removing rate δ, which means that removing rate δ has a higher impact on the disease outbreak probability than the indirect infection rate β_{ind}.

Conclusion

The current study has developed an infectious disease spread model to evaluate the impact of the different contact structures on FMD outbreaks among farms in southwest Kansas, US. Based on a farm-level, weekly-resolution temporal network of direct contacts and indirect contacts, FMD spreading scenarios are simulated and analyzed by considering 1) only direct contacts, 2) only indirect contacts, 3) their combination. We verify that disease can hardly spread among farms on a single contact-type network. The direct contacts influence the disease outbreak probability; the indirect contacts can increase the epidemic size when incorporating with the direct contacts. The study further reveals that even if there are farms which work as super-spreaders of the disease, immunizing only these farms is not enough to stop the disease. What's more, cleaning the vehicles and other equipment shared with other farms frequently to reduce the infection rate for indirect contacts is important, and early detection and isolation of infected farms can greatly reduce the epidemic size.

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Nodal Transition Graph

Cattle Movement Network

Truck Movement Network

Fig 1

Fig 2

Fig 3

Fig 4

Fig 5

Fig 6

Fig 7