

# Mathematical modeling for real epidemics situations. The case of classical swine fever virus.

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## Resumen

In this work, we describe a model to simulate the spread of within- and between- farms transmission of Classical swine fever virus (CSFV). It is a spatial hybrid model, based on the combination of a stochastic individual based model for between-farm spread with a Susceptible-Infected model for within- farm spread. An important characteristic of this model is the use, as an input, of the information available in real databases. The aim of this model is to quantify the magnitude, duration and risk zones of potential CSFV epidemics to provide support for the decision making process in future CSFV outbreaks. Model parameters and assumptions are provided and an illustration of the model's results is performed by using available data from the Spanish region of Segovia. The outputs are also compared with those given by another model.

**Keywords:** Epidemiological modeling; Individual Based model; Risk Analysis; Classical Swine Fever.

## 1. Introduction

Modeling and simulation are important tools to fight diseases [1]. Each disease has its own characteristics and, therefore, most of them need a well-adapted mathematical model in order to be able to tackle real-life situations.

In this article, we consider the Classical Swine Fever (CSF). CSF is a highly contagious viral disease of domestic and wild pigs caused by the Classical Swine Fever Virus (CSFV) [7]. It generates important economical losses (as infected pigs cannot be commercialized) in the affected regions [10]. Despite the efforts to control and eradicate CSF, this disease remains endemic in many countries of America, Africa and Asia and sporadic outbreaks have been affecting half of the European countries from 1996 to 2007 [8, 3]. Due to the different ways of CSFV spread (airborne, contact with infected animals, etc.) [3], it is difficult to extrapolate the routes of infection and consequences of a CSF epidemic from one region to another. Furthermore, the magnitude and duration of a CSF epidemic

change depending on the epidemiological and demographic characteristics of the infected region and the timing and effectiveness of the applied control measures [5, 7, 11].

The study of the potential spread patterns of CSFV into a region may help to identify risk areas to improve the prevention and management of future outbreaks. In CSF-free areas, a good way to quantify the magnitude of potential CSF epidemics and evaluate the efficiency of different control measures is to use mathematical models. Recently, some models have been developed to simulate CSFV spread into CSF-free regions such as Germany, Netherlands and Spain [5, 6, 8]. However, most of those models only focus on the between-farm spread of the CSFV, with poor assumptions regarding the within-farm spread and do not explicitly consider the specific farm to farm contact patterns (such as commercial network, shared vehicles, etc.) into the studied region.

In this work, we consider a spatial hybrid model, called Be-FAST (Between-Farm-Animal Spatial Transmission), used to simulate both within-farm and between-farm CSFV spreads and to provide CSFV risk maps of the considered region. This model is based on the combination of a stochastic Individual Based model [5], simulating the between-farm spread, with a Susceptible-Infected model [1, 6], simulating the within-farm spread. It has been previously described from the veterinarian point of view (i.e., choice of the CSFV transmission routes to be modeled or neglected, interpretation of the results, etc.) in [9].

Here, after recalling in Section 2 the main characteristics of the CSF, we give an extended description of the Be-FAST model from the mathematical perspective (i.e., detailed equations, numerical schemes, etc.) in Section 3. Finally in Section 4, in order to validate our model, we consider numerical experiments, based on real databases (i.e., farms description, commercial network, etc.) of the Spanish region of Segovia provided by the Regional Government of Castilla and Leon and the Spanish Ministry of the Environment and Rural and Marine Affairs [2]. We compare the results given by our model with those obtained with another model, namely InterSpread Plus, considering the same simulations. Moreover, we also take into account real data observed during a real CSF outbreaks in this region [8].

## 2. Classical Swine Fever characteristics

In order to help in the understanding of the Be-FAST model, described in Section 3, we briefly explain the CSF evolution process, the routes of transmission and present some control measures used to fight CSFV. A complete justification of the assumptions and simplifications described in this Section, and considered in our model, can be found in [9].

## 2.1. CSF evolution

CSF results from infection by CSFV, a member of the genus Pestivirus and family Flaviviridae [7]. CSFV affects both domestic and wild pigs. When a pig is not infected by CSFV, it is categorized in the Susceptible state (denoted by  $S_p$ ). Once it is infected, it passes successively through the following states [10]:

- Infected (denoted by  $I_p$ ): The pig is infected by CSFV but cannot infect other pigs and have no visible clinical signs (fever, lesion, etc.). The mean duration of a pig in this state is 7 days and it is called latent period. Then, it passes to be infectious.
- Infectious: The pig can infect other pigs but does not have clinical signs. The mean duration from infectious to the development of clinical sign is 21 days and it is called incubation period. Then, the pig has clinical signs.
- Clinical Signs: The pig develops visible clinical signs and still infect other pigs. After a period between two weeks and three months the pig can be recovered or died due to the disease.

We note that, the CSF death and recuperation of pigs are assumed to be neglected, because the time period considered in our simulation is short ( $\leq$  one year) and the slaughter of infected animals is considered.

Those four states can be also applied at the farm level by considering that a farm is [5]: If all pigs in the farm are in the susceptible state the farm is classified as Susceptible (denoted by  $S_f$ ); If at least one pig is in the infected, infectious or clinical signs state the farm is classified as Infected (denoted by  $I_f$ ), Infectious (denoted by  $T_f$ ) or Clinical Signs (denoted by  $C_f$ ), respectively. A farm either in the state  $I_f$ ,  $T_f$  or  $C_f$  is assumed to be a contaminated farm. Moreover, a farm in the state  $T_f$  or  $C_f$  is considered as a spreading farm.

## 2.2. Routes of transmission

The main ways of CSFV spread (i.e., that a susceptible pig becomes infected) are the following [3]: by contact with an infected animal (this way of spreading is called direct contact and, by opposition, all the other routes of spreading are referred to as indirect contacts); by contact with contaminated fomites such as vehicles, materials or peoples (in particular, veterinarians, visitors or neighborhood farmers); by airborne spread. Other alternative routes have been neglected here [3].

## 2.3. Control measures

Once an animal becomes infected, another important concept in epidemiology is its detection and application of control measures by the authorities [10].

When an infected pig is detected in a farm, this farm is classified as Detected. Generally, in a zone free of CSFV (i.e., before the detection of the first

contaminated farm, called index case), the detection occurs when pigs present clinical signs and is due to the awareness of the own farmers or private veterinarians [7]. When the first farm is detected, the awareness of the farmers and authorities is widely increased and the detection delay decrease [5]. Moreover, the detection can be also due to the control measures presented below.

Finally, in order to control a potential CSF epidemic, some measures defined by the European and Spanish legislation, described in [2] and in Section 3.6, are considered here:

- Movement restrictions: Outgoing or incoming movements in farms inside the considered region are limited during a specified time interval.
- Zoning: Zones, called control and surveillance zones, are defined around a detected farm. Surveillance activities are applied within those zones during a fixed time period.
- Depopulation: All the animals of a detected farm are slaughtered.
- Tracing: Tracing activities involve the process of determining contacts that have left or entered a detected farm during a time interval preceding the detection.

### 3. Mathematical description of the model

In this Section, we describe in detail the Be-FAST model. First, we present the general structure of our model. Then, one by one, we introduce the mathematical formulation of all the Be-FAST processes related to the input parameters, the within-farm and the between-farm CSFV spread and the control measures.

#### 3.1. General description

The Be-FAST model is used to evaluate the daily spread of CSFV within and between farms into a specific region.

At the beginning of the simulation, the model parameters are set by the user. Those referring to farms and transport of pigs are described in detail in Section 3.2. The other ones are described in Sections 3.3-3.6. Furthermore, control measures, presented in Section 2.3, are also implemented and can be activated/deactivated, when starting the model, in order to quantify their effectiveness to reduce the magnitude and duration of the CSF epidemic.

The Be-FAST model is based on a Monte Carlo approach that generates  $N_S \in \mathbb{N}$  possible epidemic scenarios (i.e., evolution of the CSFV). More precisely, at the beginning (i.e., at time  $t = 0$ ) of each scenario, denoted by  $(SCE_m)$  with  $m = 1, 2, \dots, N_S$ , all the farms are in the susceptible state except one randomly selected farm, which is assumed to have one infectious pig and is classified as infectious. Then, during a time interval  $[0, T_{\max}]$ , with  $T_{\max} \in \mathbb{N}$  a maximum simulation day number, the within-farm and between-farm daily spread

routines, described in Sections 3.3 and 3.4, respectively, are applied. Moreover, a daily process simulating the detection of contaminated farms by authorities and a daily process modeling the activated control measures, presented in Sections 3.5 and 3.6, respectively, are also run. If, at the end of a simulation day, the CSF epidemic disappears, the scenario ( $SCE_m$ ) is stopped and we start the next scenario ( $SCE_{m+1}$ ).

When the simulation is over (i.e., the scenario ( $SCE_{N_s}$ ) is finished), many kind of outputs can be generated (see Section 4.1 for some examples).

### 3.2. Farm and transport of pigs inputs

We consider a study region containing  $N_{fr} \in \mathbb{N}$  farms. For each farm, identified as farm number  $i$  (also called, in order to simplify the notations, farm  $i$ ), with  $i = 1, \dots, N_{fr}$ , the following data are given: the geographical location (i.e., latitude and longitude) of the farm centroid; the number of pigs at the first day of the simulation ( $t = 0$ ), denoted by  $SDA_i \in \mathbb{N}$ ; the type of production of the farm denoted by  $T_i \in \mathbb{N}$ : Farrowing (young pigs), Fattening (adult pigs) or Farrow-to-Finish (mixed pigs) [6]. the integrator group (i.e., groups of farms who share material and vehicles) identifier; the Sanitary Defense Association (SDA) group (i.e., groups of farms who share veterinarians) identifier.

Furthermore, the following information of all farm to farm pig shipments, occurring during a specific time interval (here, in Section 4.1, the year 2008), are also provided: the number of pigs shipped; the date of the shipment; the farms of origin and destination of the shipment.

### 3.3. Within-farm CSFV spread

The daily CSFV spread within a particular contaminated farm  $i$  is modeled by using a discrete time stochastic Susceptible-Infected (SI) model [1, 6]. The pigs in this farm are characterized to be in one of those two states: Susceptible or Infected, described in Section 2.1. In order to reduce the computational complexity of our model, the Infectious and Clinical Signs states are simulated only at the farm level (more details are given in Section 3.4). Because the time period considered is shorter than one year, the natural pig mortality is also neglected.

Under those assumptions, the evolution of  $S_{p,i}(t)$  and  $I_{p,i}(t)$ , denoting the number of susceptible and infected pigs in farm  $i$  at time  $t$ , respectively, is given (in a continuous version) by

$$\frac{dS_{p,i}(t)}{dt} = -\beta_i \frac{S_{p,i}(t)I_{p,i}(t)}{S_{p,i}(t) + I_{p,i}(t)}, \quad \frac{dI_{p,i}(t)}{dt} = \beta_i \frac{S_{p,i}(t)I_{p,i}(t)}{S_{p,i}(t) + I_{p,i}(t)}, \quad (1)$$

where  $\beta_i \in \mathbb{R}$  is the daily transmission parameter set to  $\beta_{far} = 0.66$ ,  $\beta_{fat} = 0.40$  or  $\beta_{ff} = 0.53$  depending of the farm type  $T_i$ : Farrowing, Fattening or Farrow-to-Finish pig farms, respectively [6].

System (1) is discretized by considering a time step of one day.

### 3.4. Between-farm CSFV spread

The CSFV spread between farms is modeled by using a spatial stochastic Individual Based model [5]. In this model, farms are classified in one of those four states: Susceptible ( $S_f$ ), Infected ( $I_f$ ), Infectious ( $T_f$ ) and Clinical signs ( $C_f$ ). Those states are described in Section 2.1.

The daily transition from a particular farm state to other state is modeled by considering direct contacts, indirect contacts and the natural evolution of the CSF presented in Sections 2.1 and 2.2. Those transition processes are described in detail in Sections 3.4.1-3.4.3.

#### 3.4.1. State transition due to direct contacts

The CSFV spread by direct contacts is assumed to occur due to the movements of infected pigs between farms. Those movements are estimated by using the data of the shipment of pigs introduced in Section 3.2. Since the transports of pigs are similar from one year to another [2], we generate random movements, respecting the database behavior (with data from previous years), instead of using the exact ones.

More precisely, at each simulation day  $t$ , we simulate those shipments by performing this process:

We compute  $ENM(t)$ , the estimated number of movements occurring during the simulation day  $t$ , by considering a Poisson distribution with mean  $NM(t)$ , where  $NM(t) \in \mathbb{N}$  is the number of movements occurring at day  $t$  in our database. Then, for each simulated movement:

We select randomly the farm of origin of the movement  $i \in [1, \dots, N_{fr}]$  and the farm of destination of the movement  $j \in [1, \dots, N_{fr}]$ , with  $j \neq i$ , by considering the discrete probability  $\mathbb{P}_M$ , computed once before the simulations and only each time we get a new database (we note that other parameters related to the database may be calculated once before running the model), defined by:

$$\mathbb{P}_M((i, j) = (k, l)) = \frac{M_{\text{mov}}(k, l)}{\sum_{m=1}^{N_{fr}} \sum_{n=1, n \neq m}^{N_{fr}} M_{\text{mov}}(m, n)}, \quad (2)$$

where  $k \in [1, \dots, N_{fr}]$ ,  $l \in [1, \dots, N_{fr}]$ ,  $k \neq l$  and  $M_{\text{mov}}(k, l) \in \mathbb{R}$  is the number of movements from farm  $k$  to  $l$  in the database plus  $10^{-6}$  (to take into account, with a low probability, possible movements not occurring in our database).

The, we compute  $np_{(i,j)}(t) \in \mathbb{N}$ , the number of pigs moved during this movement from farm  $i$  to farm  $j$ , by considering:

$$np_{(i,j)}(t) = \min \left\{ \text{Ceil} \left( \overline{np_{(i,j)}} \frac{S_{p,i}(t) + I_{p,i}(t)}{N_i(0)} \right), S_{p,i}(t) + I_{p,i}(t) \right\}, \quad (3)$$

where  $\overline{np_{(i,j)}} \in \mathbb{R}$  is the mean number of pigs moved between those farms in our database and  $\text{Ceil}(x)$  returns the nearest integer greater or equal to  $x \in \mathbb{R}$ . In the case of no movement from farm  $i$  to farm  $j$  in the database,  $\overline{np_{(i,j)}}$  is set to the mean number of moved pigs, considering all the database movements.

Finally, we move  $np_{(i,j)}(t)$  pigs from the origin farm  $i$  to the destination farm  $j$ . Those pigs are selected randomly in  $S_{p,i}(t)$  and  $I_{p,i}(t)$ , considering that each pig has the same probability to be selected than the other ones. We denote by  $np_{(i,j),S}(t) \in \mathbb{N}$  and  $np_{(i,j),I}(t) \in \mathbb{N}$  the number of susceptible and infected pigs that are moved during the simulated shipment, respectively. In addition, if  $np_{(i,j),I}(t) > 0$ , the state of farm  $j$  is set to the state of farm  $i$  in the following cases: the state of farm  $j$  is  $S_f$ ; the state of farm  $j$  is  $I_f$  and the state of farm  $i$  is  $T_f$  or  $C_f$  or ; the state of farm  $j$  is  $T_f$  and the state of farm  $i$  is  $C_f$ . In all other cases, the state of farm  $j$  remains unchanged.

### 3.4.2. State transition due to indirect contacts

As specified in Section 2.2, the CSFV spread due to indirect contacts is assumed to occur by either movements of vehicles transporting pigs, movements of vehicles transporting products, movements of SDA persons or the so called 'local' spread (i.e., spread due to contacts with the neighborhood which include: airborne spread and contacts with contaminated persons and fomites in the vicinity).

In Paragraphs *A-D*, we describe in detail those four kinds of indirect contacts and the way they contribute to the CSFV spread from farm to farm. Then, in Paragraph *E*, we show how this spread affects farms at the level of pig number and state.

#### A- Movements of vehicles transporting pigs:

We consider the same movements as the ones generated in Section 3.4.1. If the farm of origin of the transport is either in the state  $T_f$  or  $C_f$ , the truck transporting pigs is considered as contaminated and, thus, can infect the farm of destination. In that case, we assume that the probability of CSFV infection in the farm of destination due to contact with the contaminated vehicle is modeled by using a Bernoulli distribution with mean 0.011 [11].

#### B- Movements of vehicles transporting products:

Contacts with vehicles transporting products from farm to farm (also called integrator vehicles) are assumed to occur only among the farms belonging to the same integrator group and with the following assumptions:

- The daily number of contacts with integrator vehicles per farm is assumed to be Poisson distributed with a mean of 0.4 [5].
- An integrator vehicle can visit a maximum of 4 farms per day [2].
- An integrator vehicle is contaminated if, previously, it has visited a spreading farm (i.e., a farm either in the state  $T_f$  or  $C_f$ , see Section 2.1) [5, 11].
- The probability of CSFV infection in a farm per contact with a contaminated integrator vehicle is modeled by using a Bernoulli distribution with mean 0.0068 [11].

Thus, for each simulation day, we build the routes of those integrator vehicles and simulate the way they spread CSFV by considering the following process:

For each integrator groups  $INT$ , we perform those steps:

- For each farm in  $INT$ , we compute the number of integrator vehicles visiting it by using a Poisson distribution with mean 0.4.
- Then, we list the farms that are visited by integrator vehicles and we rearrange this list, denoted by  $L_{INT}$ , randomly (taking into account that a same farm cannot be visited two times consecutively).
- Next, a first vehicle is sent to visit the first four farms in  $L_{INT}$ , following the list order. Each fourth farm, until the end of  $L_{INT}$ , we consider a new integrator vehicle (non contaminated) starting from the next farm in  $L_{INT}$ .
- During each simulated trip, a vehicle becomes contaminated at the moment it visits a spreading farm and can infect other farm by considering a Bernoulli distribution with mean 0.0068.

### C- Movements of SDA persons:

The CSFV spread by contact with SDA persons visiting farms is assumed to occur only between farms belonging to the same Sanitary Defense Association (SDA) group.

The same process used in Paragraph B, to model the movements of integrator vehicles, is applied to simulate those contacts with the following parameters: The daily number of SDA people contacts per farm is assumed to be Poisson distributed with a mean of 0.3 [5]; a SDA person can visit a maximum of 3 farms per day [2]; a SDA person can only be contaminated if, previously, he has visited a spreading farm [5, 11]; the probability of CSFV infection in a farm per contact with a contaminated SDA person is modeled by using a Bernoulli distribution with mean 0.0065 [11].

### D- Local spread:

The CSFV local spread is assumed to occur to farms in the proximity of a farm either in the state  $T_f$  or  $C_f$ . It is mainly due to the airborne spread and contacts with contaminated neighborhood persons and fomites.

In our case, the daily probability of CSFV infection in a farm  $j$  due to the local spread from a spreading farm  $i$  at simulation day  $t$  is modeled by considering a Bernoulli distribution with mean  $(I_{p,i}(t)/\overline{N(0)})LSM(d(i, j))$ , where  $\overline{N(0)} = (\sum_i N_i(0))/N_{fr}$  is the mean number of pigs per farm at day 0,  $d(i, j)$  is the distance between farms  $i$  and  $j$  and  $LSM(x) \in [0, 1]$  is the mean daily probability of CSFV infection due to local spread between two farms at a distance of  $x > 0$  (in meter). Moreover,  $LSM(x)$  is build by interpolating the data presented in Table 1 [5].



Cuadro 1: Interpolation points used to compute  $LSM(x)$  in function of the farms distance  $x$  (in meter) [5].

Distance in meter	0	150	250	500	1000	2000
$LSM$	0.02	0.014	0.009	0.0038	0.0019	0

#### E- New infection and state transition:

For each new CSFV infection occurring in farm  $j$  during the processes described in Paragraphs  $A$  to  $D$ , if  $S_{p,j}(t) \geq 1$ , we infect one new pig in farm  $j$ . Furthermore, if the state of farm  $j$  is  $S_f$ , we change it to  $I_f$ .

#### 3.4.3. State transition due to CSF natural evolution

According to the characteristics of the CSF evolution described in Section 2.1, we consider the following changes in the farm state [5]: when a farm reach the state  $I_f$ , it will pass at state  $T_f$  after a latent period that follows a Poisson distribution with mean 7 days; when a farm reach the state  $T_f$ , it will pass at state  $C_f$  after an incubation period that follows a Poisson distribution with mean 21 days.

### 3.5. Contaminated farm detection

As specified in Section 2.3, a contaminated farm is generally detected by the observation of the clinical signs of its pigs (i.e., the farm is in state  $C_f$ ) [7]. Before detecting the index case, for each farm in the state  $C_f$ , the probability of detection per day is modeled by using a Bernoulli distribution with mean 0.03 [5]. After detecting the index case, as the awareness of the farmers and private veterinarians increase, the daily probability of detection of a farm in the state  $C_f$  is increased and is simulated by considering a Bernoulli distribution with mean 0.06 [5]. Furthermore, a contaminated farm can be also detected due to the control measures presented in Section 3.6.

### 3.6. Control measures

We now describe the control measures, introduced in Section 2.3, implemented in our model.

#### 3.6.1. Movement restrictions

A drastic restriction on movements (outgoing or incoming on farms) is applied to detected farms. Restrictions on transports of animals, integrator vehicle movements and SDA people movements in the detected farms are assumed to be Bernoulli distributed with a mean of 0.99, 0.95 and 0.8, respectively (i.e.,

movements are reduced by 99 %, 95 % and 80 %, respectively). Furthermore, after each detection, a general movement restriction, considering the three kinds of movements, is applied to all farms during a period of 90 days and following a Bernoulli distribution with mean 0.4 [2].

### 3.6.2. Zoning

The farms at a distance of less than 3 km of a detected farm are set in a control zone, whereas the farms at a distance between 3 km and 10 km of a detected farm are set in a surveillance zone [2].

A movement restriction is applied during 30 days to farms in control zones and 40 days to farms in surveillance zones [2]. In both cases, pig transports, movements of SDA persons and movements of integrator vehicles are randomly reduced by considering a Bernoulli distribution with mean 0.95, 0.9 and 0.7, respectively [2]. Overlapping of the movement restrictions of control and surveillance zones is allowed (i.e, if a farm has an active movement restriction, we add the days of the new restriction to those of the old restriction).

Furthermore, we apply another surveillance process to the farms within those zones, in addition to the one described in Section 3.5. The daily probability detection of a farm  $j$  in the state  $C_f$  due to this surveillance is assumed to be dependent of the proportion of infected animals and modeled by considering [2] a Bernoulli distribution with mean  $\alpha \frac{I_{p,j}(t)}{S_{p,j}(t) + I_{p,j}(t)}$  where  $\alpha$  is set to 0.98 or 0.95 if the farm  $j$  is within a control zone or within a surveillance zone and is not within a control zone, respectively.

### 3.6.3. Depopulation

The depopulation (i.e., the slaughter of all animals) of a detected farm  $i$  occurs after a random time period, generated by using the data provided by Table 2 [3], starting from the day of its detection. However, the maximum number of farms to be depopulated per day is assumed to follow a Poisson distribution with mean 20 [2]. Thus, if this limit is reached, the farm is depopulated the following days. When the farm  $i$  is depopulated, its number of pigs is set to 0 and it is not considered anymore by the model. Then, after a time period following a Poisson distribution with mean 90 days [2], the farm is repopulated (i.e., new pigs are introduced): the number of susceptible pigs is  $N_i(0)$ , the farm state is set to  $S_f$  and the farm is again taken into account by the model.

Number of days	0	1	2	3	4	5	6	7
Probability	0.11	0.58	0.2	0.06	0.04	0.004	0.003	0.0030

Cuadro 2: Probability distribution of the number of days to wait before depopulating a detected farm [3].

### 3.6.4. Tracing

The objective of tracing is to identify infectious contacts which may have introduced CSFV into a detected farm or spread CSFV to other farms. We include the tracing of all contacts (i.e., farms sending or receiving animals, sharing SDA persons or sharing integrator vehicles) of a detected farm occurring 60 days before the detection [2]. However, due to failures in the administrative system (error in databases, lack of personnel, etc.) tracing all the contacts is not always possible.

More precisely, when a farm  $i$  is detected, we list all the farms who have shared, 60 days before the detection, at least one integrator vehicle, one SDA person or one transport animal vehicle with farm  $i$ . Then, for each farm in this list, we decide if it is traced or not according to following probabilities: the probability of tracing a farm due to animal transport, integrator vehicle movement or SDA people movement is assumed to be Bernoulli distributed with a mean of 0.99, 0.7 and 0.4, respectively [2]. Next, for each farm to be traced, we select the day of tracing, taking into account, as in Section 3.6.3, that the maximum number of farms to be traced per day is assumed to follow a Poisson distribution with mean 60. Finally, we perform a detection process to the traced farms, the day of their tracing, by considering that the probability of detecting a contaminated traced farm follows a Bernoulli distribution with mean 0.95 [2].

## 4. Model Validation

In order to validate the Be-FAST model, we perform various numerical experiments, described in Section 4.1. Those experiments are also run by considering a commercial epidemiological model, called InterSpread Plus, briefly introduced in Section 4.2. Finally, in Section 4.3, the results obtained by both models are compared between them and with data observed during a real CSF outbreaks occurring in Spain [8].

### 4.1. Numerical experiments

We consider the province of Segovia, one of the most important areas of pig production in Spain, which have a surface of 6796 km<sup>2</sup>. A real database, provided by the Spanish Regional Government of Castilla and Leon and the Spanish Ministry of the Environment and Rural and Marine Affairs [2], corresponding to the inputs, described in Section 3.2, of the year 2008 is used.

In the experiments considered in this paper, all the control measures described in Section 3.6 are activated and the model is running with  $N_S = 1000$  scenarios during a maximum period of  $T_{\max} = 1095$  days, which is large enough to ensure the end of the CSF epidemic [9].

After each experiment (i.e., the scenario ( $SCE_{N_S}$ ) is over), many kinds of outputs can be obtained. Here, we consider a typical output referring to risk management [5]. More precisely, for each farm  $i$ , we compute its risk of CSFV

introduction, denoted by  $RI(i)$ . It is defined as the number of times that farm  $i$  becomes contaminated during the whole Monte-Carlo simulation. In particular, in order to identify the risk zones in the studied region, we are interested in obtaining the geographical distribution of  $RI$ . Typically [8], the risk zones are classified in three categories: high, medium and low risk. This is useful, for instance, to design preventive control measures to fight CSFV (see Section 5 for more details). To do so, and to compare the values of  $RI$  given by the models presented in Section 4.2, we first normalize  $RI(i)$  by considering  $\bar{RI}(i) = \frac{\hat{RI}(i)}{\max_i \hat{RI}(i)}$  where  $\hat{RI}(i) = RI(i) / \left( \sum_i RI(i) \right)$ . Then, we obtain the spatial distribution of  $\bar{RI}$ , in Segovia, by interpolating the values of  $\bar{RI}(i)$  considering an Inverse Distance Weighted method. Finally, the identification of the three risk zones is done by considering the Jenks Natural Breaks (JNB) classification method [4].

## 4.2. Considered models

In order to validate the BE-FAST model, we perform the experiments, presented in Section 4.1, by using the two models:

A MatLab Ver. 2009.a (<http://www.mathworks.com/>) script implementation of the Be-FAST model. This model is denoted by **BF**.

We also consider the InterSpread Plus software Ver. 1.0.49.5 (<http://www.interspreadplus.com/>). InterSpread Plus is a commercial C++ implementation of a state transition model [12]. It is one of the most popular epidemiological model software used in the world. However, in our opinion, it has several drawbacks, as, for instance, the low transparency of the code (it is a black-box program) and the difficulty to incorporate complex databases with real movements or contacts from farm-to-farm. We intend to reproduce the same processes as the one used by the Be-FAST model. The main differences between both model were: InterSpread Plus does not allow to model the within-farm transmission (it is a purely between-farm spread model), the model coefficients cannot be expressed in function of the number of infected or susceptible pigs; the real commercial networks (i.e., pig shipments, SDA groups and integrator groups) cannot be integrated directly in InterSpread Plus. It has been simplified by creating random routes taking into account the distance between farms.

## 4.3. Results

The  $\bar{RI}$  risk maps generated by models **BF** and **IS**, for the considered experiment, are presented in Figure 1. The considered Jenks Natural Breaks (JNB) classification, containing (for a better understanding of the maps) 9 intervals corresponding to 9 gray colors, is also reported in this Figure: the first three intervals [0-0.07] correspond to the low risk areas; the intervals [0.07-0.15] correspond to the medium risk areas; and the last three intervals [0.15-1] correspond to the high risk areas.

In order to compare the results given by models **BF** and **IS**, we have considered the data of the CSF epidemic in Segovia occurring in 1997-98 provided by [2]. Here, we consider the geographical position of the infected farms to validate the risk maps generated by **BF** and **IS** models. In Figure 1, we incorporate those farms to the **BF** and **IS** risk maps and we detail the zone where most of the farms are included.

We can see that, in the **BF** case, most of the infected farms are situated in a dark (high risk) zone and other farms in medium or low risk zones. In the **IS** case, the high risk zone does not include those farms, and the farms are mainly located in low risk areas. The mean  $\bar{RI}$  value of the 1998-97 infected farms given by **BF** model is 0.201, which corresponds to the highest risk in the considered JNB classification. In the **IS** model, the mean risk value of those farms is 0.032, which is included in the low risk area. This result tends to show that the maps generated by model **BF** are more consistent with real data than those generated with model **IS**. This can be explained by the fact that our model uses the real commercial network (i.e., transport of animals, SDA and integrator groups) between farms, whereas this information is not suitably processed by **IS**. This shows the importance of the use of this database to obtain a fine representation of the risk areas, and one should use this input in an epidemiological model as soon as it is available. We point out the fact that 10 years separate the used databases and the 1997-98 outbreak in Segovia, explaining why some farms could be included in low risk zones, even in the **BF** map. However, this also shows the robustness of the **BF** risk maps, which seem to be valid for years different from those generating the database.

## 5. Conclusions

During this work, we have given an extended mathematical description of the spatial model called Be-FAST, used for the study of CSFV spread into a region. The principal originality of this model is that it combines a Susceptible-Infected model, for the within-farm spread process, with an Individual Based model, for the between-farm spread process. The proportion of infected animals given by the Susceptible-Infected model is used to calibrate some coefficients of the Individual Based model. Another important feature of the model, is the possibility of using of a real database of the commercial network between farms. We have seen, when comparing the results given by the model Be-FAST with those obtained by real outbreaks data, that these new characteristics are very important for the identification of the risk zones.

One of the next steps will be to include the economical aspects (for instance, the prices of pigs, control measures, etc.) and to use the risk map distribution to design CSF preventive campaigns, in order to reduce the economical impact and the risk of possible future outbreaks.

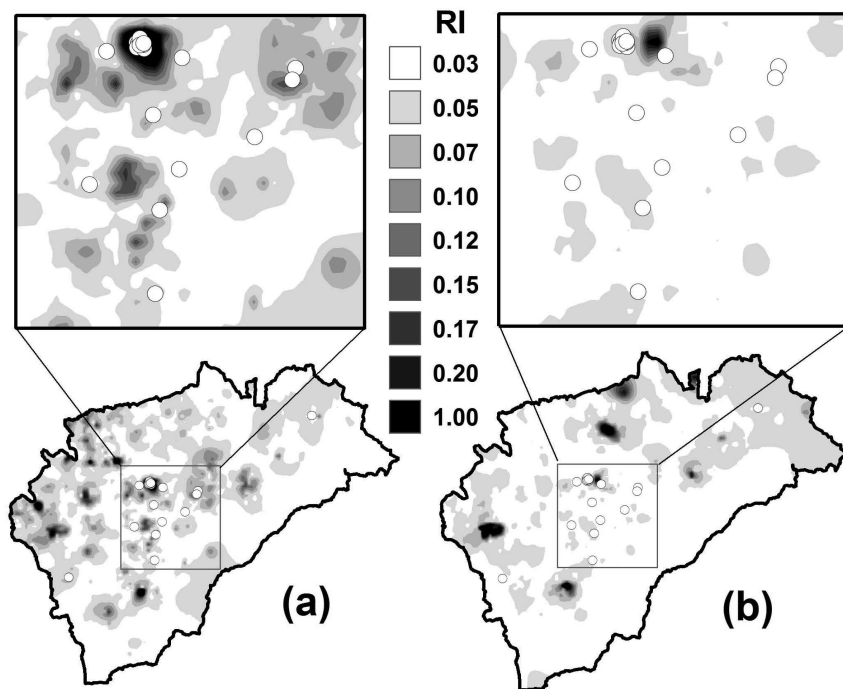


Figure 1: Interpolated  $\bar{R}I$  maps obtained by models (**LEFT**) **BF** and (**RIGHT**) **IS** for the considered experiment. We also report, with white spots ( $\circ$ ), the location of the farms infected during the 1997-98 CSF epidemic in Segovia. Furthermore, we present, in the square region, a zoom of the zone where most of those farms are situated (except two of them). The considered JNB classification is also reported.

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## Bibliografía

- [1] R.M. Anderson and R.M. May. Population biology of infectious diseases: Part 1. *Nature*, 280:361–367, 1979.
- [2] Junta de Castilla y Leon and Ministerio de Agricultura Pesca y Alimentacin. Expert opinion elicitation performed for foot-and-mouth disease and classical swine fever with the veterinary services. web site: <http://www.jcyl.es> and <http://www.marm.es>, 2008.
- [3] A.R.W. Elbers, A. Stegeman, H. Moser, H.M. Ekker, J.A. Smak, and H. Pluimers. The csf epidemic 1997-1998 in the netherlands: descriptive epidemiology. *Prev. Vet. Med.*, 4:157–184, 1999.
- [4] G.F. Jenks. The data model concept in statistical mapping. *International Yearbook of Cartography*, 7:186–190, 1967.
- [5] S. Kartsen, G. Rave, and J. Krieter. Monte carlo simulation of classical swine fever epidemics and control i. general concepts and description of the model. *Vet. Microbiol.*, 108:187–198, 2005.
- [6] D. Klinkenberg, J. De Bree, H. Laevens, and M.C.M. De Jong. Within- and between-pen transmission of csf virus: a new method to estimate the basic reproduction ratiom from transmission experiments. part 1. *Epidemiol. Infect.*, 128:293–299, 2002.
- [7] F. Koenen, G. Van Caenegem, J.P. Vermeersch, J. Vandenheede, and H. Deluyker. Epidemiological characteristics of an outbreak of classical swine fever in an area of high pig density. *Vet. Record*, 139(15):367–371, 1996.
- [8] B. Martínez-Lopez. *Desarrollo de modelos epidemiológicos cuantitativos para el análisis del riesgo de introducción y difusión potencial de los virus de la fiebre aftosa y de la peste porcina clásica en España*. PhD thesis, Universidad Complutense de Madrid, Facultad de Veterinaria, Spain, 2009.
- [9] B. Martínez-Lopez, B. Ivorra, A.M. Ramos, and J.M. Sánchez-Vizcaíno. A novel spatial and stochastic model to evaluate the within and between farm transmission of classical swine fever virus: 1. general concepts and description of the model. *Vet. Microbiol.*, 147(3):300–309, 2011.
- [10] V. Moennig. Introduction to classical swine fever: virus, disease and control policy. *Vet. Microbiol.*, 73(2):93–102, 2000.
- [11] A. Stegeman, A.R.W. Elbers, A. Bouma, and M.C.M. De Jong. Rate of inter-farm transmission of classical swine fever virus by different types of contact during the 1997-8 epidemic in the netherlands. *Epidemiol. Infect.*, 128:285–291, 2002.
- [12] M. Stern. *InterSpread Plus User Guide*. Institute of Veterinary, Animal, and Biomedical Sciences, Massey University, Palmerston North, New Zealand., 2003.