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## A model for the operations to render epidemic-free a hog farm infected by the Aujeszky disease

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### Abstract

We present here a case study for modelling the control of the Aujeszky disease, in a farm declared virus-free. The model is validated on the available data. Simulations are performed to assess different containment strategies for the epidemic. Final recommendations indicate that a strict reduction of biohazards in the farrowing unit should be enforced. Also neglecting the third inoculation in the vaccination protocol leads to a sensible and quantifiable increase of the prevalence of the disease. The findings indicate that it is more important to keep biosafety at a high level in the farrowing unit rather than strive for the highest standards in the gestation unit. Also the importance of a properly implemented vaccination appears fundamental, and its absence can be quantified via our simulations.

**Keywords:** Data Analysis, mathematical modelling, simulations, epidemics, control measures.

**AMS 2010 codes:** 92D30.

## 1 Introduction

In this joint work among mathematicians and veterinarians, a differential equations model is proposed for the operations in a specific hog raising farm. Similar models for the farm operations in other settings are known in the literature, see for instance [2, 13]. The model is validated on gathered field data, in a farm that, after monitoring lasted for more than a year, until it has been finally declared Aujeszky-disease free. Based on this

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model, then further simulations have been performed in order to assess the role that various factors which might contribute to keep the disease endemic in the environment.

The paper is organized as follows. The next Section contains background information on the disease, in Section 4 we present the model, amounting to a total of 45 differential equations, since we account for different classes, cohorts and age groups of animals, in each of the units in which the farm is subdivided. The complexity of this model prevents the assessment of any analytic result, so that it can be studied only via numerical simulations, implemented in Section 6. In it, after validation, possible different scenarios are considered for the role that the infection has on the whole dynamics of the epidemic: we look firstly at the disease in the gestation and farrowing units, secondly in the fattening units, finally we assess the impact of a badly implemented vaccination policy. A final discussion and recommendation Section concludes the paper.

## 2 Background on the disease

Aujeszky's disease (AD) is a viral widespread disease affecting most mammals, except humans and higher primates. Domestic and wild pigs represent the only natural hosts of Aujeszky's disease virus (ADV) and serve as source of infection for the other species. In all other susceptible mammals the disease has a very rapid and fatal course. In pigs the clinical features vary considerably, according to age and sex. In piglets the disease is devastating, characterized by neurological signs and fatality rates close to 100%. A note is here in order. This information refers to the "disease" in its acute or chronic form. In the present situation, what is observed in the farms is only the presence of the virus. By the way, this can be ascertained only via expensive and laborious laboratory tests, which cannot be carried over the whole set of newborns in view of the excessive time and labor required to gather the samples. This is the reason for undertaking a project like this one, when suitable abundant field data cannot be obtained at a reasonable price. The mathematical model allows the replacement of field experiments by "*in silico*" simulations, providing useful information also for the field practitioner. Further, note that the positivity to laboratory tests simply states that the animal has been exposed to the virus and that nevertheless it could potentially develop the disease. According to field experience, it is now several decades that the most acute form of the disease does not appear in the farms. Therefore the high fatality rate reported above does not apply to our situation. In addition, even if it did, we would not account explicitly for disease-related mortality of newborns in the model, since the latter is already discounted in the net birth rate data provided by our field measurements.

In older pigs the infection results mainly in respiratory signs. In pregnant sows the infection causes reproductive failure. In vaccinated animals the infection is usually asymptomatic. Lifelong latent infection commonly follows inapparent infection or clinical recovery. Stress may reactivate latent infections, causing recrudescence shedding of ADV. The primary means of transmission of the virus is thought to be by direct contact between infected and susceptible pigs. Indirect contacts by personnel, infected semen, feed, vehicles and equipment can also spread the virus within and among herds. Also long-distance airborne transmission between herds has been described [3]. Several risk factors resulted associated with the infection in different studies. These risk factors are related to management and herd characteristics such as pig production cycle, gilts replacement, herd size, animal density, vaccination schemes, biosecurity measures. Other risk factors are related to the geographic area such as AD occurrence, animal and herd density, pig transports, pork industry, feral pigs presence [1, 8–11, 14, 16–18].

The infection causes severe economic losses to all sectors of pig industry if not submitted to effective control strategies. These include application of strict biosecurity measures, marker vaccination, selective removal of infected pigs and final depopulation of residual infected herds. Based on these principles, the European Union has implemented AD eradication programmes. As a consequence in several member states the disease has been eradicated. In Italy the eradication programme has been established in 1997, when the infection was endemic with prevalences ranging from 8% in Trentino Alto-Adige Region to 81% in Lombardy, [19], but its progress has been slow and the final goal is still far from being achieved. It is therefore crucial for Italian pig industry to better understand the epidemiology of AD and to identify the weak points in herd management that hamper its

control. This study is aimed at contributing to this goal, analyzing the effect of different policies and measures of biohazard containment on the behavior of ADV infection in this typical farrow-to-finish pig herd.

### 3 The farming operations

The purpose of our model is to reproduce exactly how the farm in which our data have been collected operates.

Each individual animal, sows, newborns and pigs in the weaning and fattening units of the farm, is ear-tagged and easily identifiable along the production flow. In this way the farmer can recognize it and, depending on its age, bring it into the appropriate stall at every moment that an animal movement is necessary.

The natural unit of time  $T$  for the model is one month, since it is the time spent by the sows in the farrowing unit.

In demographic age-structured mathematical population models the cohort is represented by the set of all animals of the same age; in epidemiological models it is given by all the individuals in the same stage of infection. In our model the cohort is represented by the animals in the same stage of production cycle which is strictly driven by the farmer. This starts from the artificial insemination, in which the sows are kept in different stages of the gestation cycle, so that a subset of them each month gives birth at about the same time. In the model we follow the flow of each individual cohort.

The continuous production cycle is composed by four separate units: gestation, farrowing, weaning and fattening. In each different production unit the spread of ADV may occur either by nose to nose contact, in the last three environments where the animals are freely moving and mixing, or by short distance transmission in the gestation unit. Indeed in the gestation unit, individual stalls are present, so that the sows thus occupy a fixed place. This situation is common in farms, compare for instance [2] for the case of industrial laying hens flock in which the animals are kept in long cage rows. Thus each individual sow can come hardly in contact with the other ones, except possibly the two in the confining boxes, Figure 1. However, during the cleaning operations, the sewage is swept all across the barn, so that if the infection is present somewhere in the barn, the virus easily spreads throughout the whole environment. Moreover the virus is highly volatile and airborne transmission may occur, [3]. The disease transmission is modeled by the standard incidence formulation for animal contacts modeling proportional mixing and by a linear term for the airborne infection.

Movement across the farm units occurs at discrete times, usually the beginning of the month. In what follows we will indicate it using a general notation that we introduce now. Let  $Q(t)$  be a generic population at time  $t$  in a certain unit  $A$  of the farm. Suppose that at the beginning of the  $n$ -th month it must be moved away into another unit  $B$ , where it will be called the  $P$  population and where it will live for the next stage, i.e. the  $n+1$ -st month, or the time span  $[nT, (n+1)T]$ . In view of our notation, the movement will occur at time  $nT$ . We denote by  $nT^-$  the instants immediately preceding the movement, and by  $nT^+$  those immediately following. To state that the “initial” population  $P$  of the unit  $B$  comes from the “last” population  $Q$  that lived in the unit  $A$  just before time  $nT$ , we write the equation

$$P(nT^+) = Q(nT^-). \quad (1)$$

The statement should be read right to left, like if there was an arrow:  $P(nT^+) \leftarrow Q(nT^-)$ , meaning what was population  $Q$  just before time  $nT$  now is becoming population  $P$ . Expressions like (1) will therefore be used below to give the initial conditions for the simulations in each unit.

Note that we consider the cohorts and do not model the farm using several communicating SI epidemic models corresponding to the different units in the farm, also for another fundamental reason. The communications would then be modeled via migration rates, but these represent *the fraction* of the population say in unit 1 that moves into unit 2. This implies that not all the population in unit 1 moves into the next unit, and therefore a network of SI epidemic models would not mimick what happens in the farm, where each unit is *emptied* whenever the animals are old enough.



**Fig. 1** Gestation room with individual boxes.

In the gestation unit there are four subsets of sows, each in a different month of the gestation, to suitably account for about four months of gestation time. In this way every month a new cohort of newborns is ensured, giving a continuous production cycle. At the beginning of the month one of these subsets is inseminated, while the one ready for giving birth is moved into the farrowing unit.

The sows and the newborns are all kept together in the farrowing unit, for about a month. After that, the sows return to the gestation unit to start again a new gestation cycle, while the newborns are moved into the weaning unit. A new cohort of pregnant sows now enters into the farrowing unit, and the cycle repeats.

In the weaning unit the newly entered piglets from the farrowing unit replace the oldest cohort there present, which is moved further to the fattening unit. The animals in the weaning unit enter it when they are one month old and stay there for two months, freely mixing with all other animals, Figure 2.



**Fig. 2** Weaning unit.



A similar situation occurs in the fattening unit, where the incoming animals are now three months old. The length of the stay is here about six months, and at the end the oldest cohort is sold for slaughtering. Again free mixing occurs, Figure 3.



**Fig. 3** Fattening unit, with several animals in each box.

#### 4 The mathematical model

The infection once contracted is carried for life, so the epidemiological model is necessarily of type SI (Susceptible-Infected), as no recovery is possible.

The model we present is quite complicated, since it will mimick what really happens in a farm, in which each segment of the population is kept segregated from other animals. We present now a broad overview of the situation, followed then by a detailed description of the model for each subset of the pigs population.

Typically, in the farm cohorts of animals of the same age live together, but change the living environments from time to time, as they grow older. The sows for reproduction purposes occupy an area of the farm, from which they are moved into the farrowing unit where they give birth to their offsprings, with whom they share their first weeks of life. After that, the sows are moved back into the first area, and the newborns move into another area of the farm. From there onwards, they will be living in the fattening areas of the farm.

The sows population is divided into 5 cohorts, corresponding to subsequent “waves”: one of them in turn occupies the farrowing unit while the other ones live in the gestation unit. In view of the assumption that sows live 120 days in the gestation unit and 30 days in the farrowing unit, the situation can be described by subdividing into 4 stages, each one being 30 days long: after having gone through all of them, each cohort arrives in the farrowing unit, and after an additional 30 days, it returns in the first stage of the gestation. In order to avoid confusion among the cohorts, each one of them in the simulations has been labeled with a number, from 1 to 5, the first four of which initially being in the gestation unit, and the fifth one in the farrowing unit. After a month, cohorts 2 to 5 will be present in the gestation unit, with cohort number 1 being in the farrowing unit. This scheme is repeated as time goes by.

Further, each cohort is divided into 3 subsets: the first one accounts for the vaccinated sows, in which the vaccine has worked, so that they are immune from the disease; the second one contains the vaccinated but

still susceptible ones, in which the vaccine has not been fully effective for whatever reason, either technical or biological; the last one the infected sows. Note that all the sows in the farm are vaccinated, and for this reason the model does not explicitly consider the vaccinated class for the sows. The model instead accounts for the presence of infected sows since vaccination does not completely prevent infection. The initial conditions for the 5 cohorts used in the simulations are arbitrary, but checking that their sum coincides with the number of animals in reproduction in January 2008, the month in which the set of our data sampling begins. In addition, the initial values of these cohorts are of the same order of magnitude.

#### 4.1 The gestation unit

The model for this part of the farm can now be constructed mathematically. Each cohort is represented by subscripts 1-3, then 4-6, 7-9, 10-12. Here  $x_1, x_4, x_7, x_{10}$  represent the populations of the immunized animals of each cohort, in which only natural mortality  $m$  is present. Further,  $x_2, x_5, x_8, x_{11}$  represent the susceptible animals: individuals leave this class either by natural mortality or by becoming infected, at rate  $\tau$  if the latter is due to biohazards or external factors, and at rate  $\alpha$  if this occurs via direct contact with infected individuals. Here, biohazards are represented by all those factors that are not explicitly built as variables in this model, like for instance absence of filters at the windows, lack of attention to cleanliness, rats, leakage of contaminated liquids, contact with external entities to the farm, such as trucks or people entering the farm without proper protection and so on. Note that the disease incidence is proportional to the ratio of total number of infected in the total population. Finally,  $x_3, x_6, x_9, x_{12}$  denote the infected animals, which enter into this class from the corresponding exiting terms of the susceptible class and leave via natural mortality. Letting  $X = \sum_{i=1}^{12} x_i$  represent the total animal population in this part of the farm, the equations for the gestation unit are therefore

$$\begin{aligned}\frac{dx_1}{dt} &= -mx_1; \\ \frac{dx_2}{dt} &= -mx_2 - \tau x_2 - \alpha x_2 \frac{1}{X} [x_3 + x_6 + x_9 + x_{12}] \\ \frac{dx_3}{dt} &= -mx_3 + \tau x_2 + \alpha x_2 \frac{1}{X} [x_3 + x_6 + x_9 + x_{12}]; \\ \frac{dx_4}{dt} &= -mx_4; \\ \frac{dx_5}{dt} &= -mx_5 - \tau x_5 - \alpha x_5 \frac{1}{X} [x_3 + x_6 + x_9 + x_{12}]; \\ \frac{dx_6}{dt} &= -mx_6 + \tau x_5 + \alpha x_5 \frac{1}{X} [x_3 + x_6 + x_9 + x_{12}]; \\ \frac{dx_7}{dt} &= -mx_7; \\ \frac{dx_8}{dt} &= -mx_8 - \tau x_8 - \alpha x_8 \frac{1}{X} [x_3 + x_6 + x_9 + x_{12}]; \\ \frac{dx_9}{dt} &= -mx_9 + \tau x_8 + \alpha x_8 \frac{1}{X} [x_3 + x_6 + x_9 + x_{12}]; \\ \frac{dx_{10}}{dt} &= -mx_{10}; \\ \frac{dx_{11}}{dt} &= -mx_{11} - \tau x_{11} - \alpha x_{11} \frac{1}{X} [x_3 + x_6 + x_9 + x_{12}]; \\ \frac{dx_{12}}{dt} &= -mx_{12} + \tau x_{11} + \alpha x_{11} \frac{1}{X} [x_3 + x_6 + x_9 + x_{12}].\end{aligned}$$

The initial conditions for the immunized animals are

$$\begin{aligned}x_1(nT^+) &= z_1(nT^-), & x_4(nT^+) &= x_1(nT^-), \\ x_7(nT^+) &= x_4(nT^-), & x_{10}(nT^+) &= x_7(nT^-);\end{aligned}$$

those for the susceptibles are

$$\begin{aligned} x_2(nT^+) &= z_2(nT^-), & x_5(nT^+) &= x_2(nT^-), \\ x_8(nT^+) &= x_5(nT^-), & x_{11}(nT^+) &= x_8(nT^-); \end{aligned}$$

finally for the infected we have

$$\begin{aligned} x_3(nT^+) &= z_3(nT^-), & x_6(nT^+) &= x_3(nT^-), \\ x_9(nT^+) &= x_6(nT^-), & x_{12}(nT^+) &= x_9(nT^-). \end{aligned}$$

Note that the new sows in the first cohort are those discharged from the farrowing unit,  $z_k$ , for  $k = 1, 2, 3$ .

The parameters have been chosen as follows. For natural mortality,  $m$ , the value is taken from data from the particular raising farm considered here. Moreover, since we have the data of the new acquisitions of sows, since these are accurately selected and vaccinated, we added these monthly acquisitions in the set of the immune sows of the cohort in the first stage of the gestation, since they are waiting to be inseminated. In each cohort, the deaths are assumed proportionally subdivided among their 3 subsets, susceptible, infected, immune.

## 4.2 The farrowing unit

Letting  $Z = \sum_{i=1}^3 z_i$ , the farrowing unit equations are the following ones,

$$\begin{aligned} \frac{dz_1}{dt} &= -mz_1; \\ \frac{dz_2}{dt} &= -mz_2 - \Delta z_2 - \beta z_2 \frac{1}{Z} z_3; \\ \frac{dz_3}{dt} &= -mz_3 + \Delta z_2 + \beta z_2 \frac{1}{Z} z_3; \\ \frac{du_1}{dt} &= b(z_1 + z_3); \\ \frac{du_2}{dt} &= bz_2 - \Delta u_2 - \gamma u_2 \frac{1}{Z} (z_3 + u_3); \\ \frac{du_3}{dt} &= \Delta u_2 + \gamma u_2 \frac{1}{Z} (z_3 + u_3). \end{aligned}$$

The first three equations describe the sows cohort, immunized  $z_1$ , susceptible  $z_2$  and infected  $z_3$ , the remaining ones are for the newborns again immunized  $u_1$ , susceptible  $u_2$  and infected  $u_3$ .

Clearly, the initial conditions of the last equations are zero. The initial conditions for the immunized animals are

$$z_1(nT^+) = x_{10}(nT^-), \quad u_1(nT^+) = 0;$$

those for the susceptibles are

$$z_2(nT^+) = x_{11}(nT^-), \quad u_2(nT^+) = 0;$$

finally for the infected we have

$$z_3(nT^+) = x_{12}(nT^-), \quad u_3(nT^+) = 0;$$

Note that the new sows in the first cohort are those discharged from the farrowing unit,  $z_k$ , for  $k = 1, 2, 3$ .

The first equation describes the immune sows evolution. The second one, the susceptible ones: they leave this set via natural mortality and via contagion due either to external means, at rate  $\Delta < \tau$ , since in general this

unit is much more checked and disinfected than all the other parts of the farm, or by contact with an infected, at rate  $\beta < \alpha$ , for the same reasons given above. Note that in this equation we do not take into account the contagion from infected newborns to susceptible sows, i.e.  $u_3$  is not added to  $z_3$  in the last term, because it is well known that this type of contagion cannot biologically occur, [16].

The third equation concerns the infected, which enter this class through terms arising from the infection processes described in the former equation, and leave only via mortality. The fourth equation represents the immune newborns, which are so via the maternal immunity that lasts for about 90-100 days. Only the sows which were exposed to the virus whether wild or coming from the vaccine, can give this maternal immunity protection to their offsprings. Thus this equation has net birthrate  $b$  proportional to the sum of the immune and infected sows. Note that we take the same birth rate  $b$  for both susceptible and infected sows, because as mentioned earlier, by “infected” sows we mean sows that have been vaccinated, and therefore are immune and do not experience clinical signs. Recall that, as stated in Section 2, exposure to the virus is the only way the “disease” is present in farms nowadays. Thus, in practice, no difference in the birth rates between susceptible and infected sows is observed. The fifth equation contains the susceptible newborns, coming from susceptible sows. The birthrate,  $b$ , is proportional to the number of susceptible sows. The equation presents two contagion exits: either via biohazards at rate  $\Delta$  and via direct contact with infected sows or offsprings at rate  $\gamma$ . Finally the last equation describes the infected newborns, with entries from the exits of the previous equation.

The value of the net birthrate is  $b = 0.2358$  on the basis of the available data. Note that again, the “disease” is in fact only an infection, as stated in Section 2 and thus disease-related mortality does not really arise. Therefore no disease-related mortality appears in the equation for the infected newborns  $u_3$ . To validate this choice, in the simulation we compared every four months the estimated number of newborns with the real data, see Table 2.

## 5 Model validation

To validate this part of the model, we compare the simulations with the gathered field data, see Tables 1-3.

Since we have the data on the infected sows, via serological tests, in view of the fact that these animals are systematically removed and slaughtered, we have subtracted monthly these data from the infected. To calibrate the value of the mortality rate  $m$ , every 4 months the simulated data are compared with the actual data, see Table 1.

**Table 1** Comparison between the actual and the simulated number of sows

actual number of sows: January - April	simulation
1251	1230.40
actual number of sows: January - August	simulation
2446	2424.85
actual number of sows : January - December	simulation
3652	3676.35

The discrepancy between the actual data and the simulation results is really small, of about 1.65% in the first period, down to 0.86% in the second one up to 0.67% over the whole year.

In view of the fact that the newborn numbers change significantly in each third of the year, we consider the estimate for the birth rate to be quite good, since the error in the first third is 4.26%, in the first two it drops to 1.82% and over the whole year it is 2.35%.

In addition, the newborns leave the farrowing unit after 25 days, i.e. just about a month after the mother has entered into it.

Finally, we consider that prevalence of the AD in the region in the year 2008 - 2009 dropped to about 26%, (B. Sona, et al., 2008). We therefore disregarded values of the free parameters leading to much higher preva-



**Table 2** Comparison between the actual and the simulated number of newborns

actual number of newborns January - April	simulation
1600	1668.1851
actual number of newborns January - August	simulation
3450	3512.6317
actual number of newborns January - December	simulation
5160	5281.3771

lence percentages than these. Considering the following choice of the free parameters:  $\alpha = \xi = 0.006$ ,  $\beta = 0.002$ ,  $\gamma = \eta = 0.004$ ,  $\tau = S = Q = 0.003$ ,  $\Delta = 0.002$ .

Table 3 contains the results of the simulations in the gestation and farrowing units of the farm.

**Table 3** Simulation of monthly percentages of infected sows

	Jan	Feb	March	April
infected sows	60.9639	70.0257	79.2916	84.6477
percentage of infected sows	19.65	22.70	25.77	27.85
	May	June	July	Aug
infected sows	85.7588	73.3416	75.5884	77.6100
percentage of infected sows	26.87	26.15	25.13	26.4000
	Sept	Oct	Nov	Dec
infected sows	77.5595	77.4896	77.1011	75.1609
percentage of infected sows	25.66	24.96	24.97	22.78

## 5.1 The weaning unit

We now describe the weaning unit. Here the weaned pigs are left for about two months, before entering the fattening unit of the farm. We subdivide the weaning unit into two classes, I and II. The weaned pigs spend about a month in each of them. In fact this subdivision is artificial, it is done for modelling purposes only, while in reality this does not occur. However it should be noted that in class II, i.e. between the 60th and 90th day of life, the first vaccination occurs. The second one will follow after another three to four weeks from the first one. Letting  $W = \sum_{i=1}^7 w_i$ , the governing equations are:

$$\begin{aligned}
 \frac{dw_1}{dt} &= -nw_1; \\
 \frac{dw_2}{dt} &= -nw_2 - Sw_2 - \eta w_2 \frac{1}{W}(w_3 + w_6); \\
 \frac{dw_3}{dt} &= -nw_3 + Sw_2 + \eta w_2 \frac{1}{W}(w_3 + w_6); \\
 \frac{dw_4}{dt} &= -nw_4 - kw_4; \\
 \frac{dw_5}{dt} &= -nw_5 - Sw_5 - kw_5 - \eta w_5 \frac{1}{W}(w_3 + w_6); \\
 \frac{dw_6}{dt} &= -nw_6 + Sw_5 + \eta w_5 \frac{1}{W}(w_3 + w_6); \\
 \frac{dw_7}{dt} &= -nw_7 + k(w_4 + w_5).
 \end{aligned}$$

The initial conditions for the immunized animals are

$$w_1(nT^+) = u_1(nT^-) + u_3(nT^-), \quad w_4(nT^+) = w_1(nT^-);$$

those for the susceptibles are

$$w_2(nT^+) = u_2(nT^-), \quad w_5(nT^+) = w_2(nT^-);$$

for the infected we have

$$w_3(nT^+) = 0, \quad w_6(nT^+) = w_3(nT^-);$$

and finally for the vaccinated ones, since none is so initially, we have

$$w_7(nT^+) = 0.$$

The first three of them describe class I, the remaining ones class II. The first equation represents the weaned pigs that were born one month earlier either from sound and well vaccinated mother, or from infected mothers, i.e. the weaned pigs who are immune from the disease in view of the action of the maternal immunity. Animals can leave this class only by death, at rate  $n$ , here chosen to equal the sows' mortality,  $n = m$ . The second equation contains the dynamics of the weaned pigs that were born from susceptible mothers, so that they are not immune from the AD. In addition to natural mortality, we must here include also an exit from the class due to contagion, either direct or by biohazard, at respective rates  $\eta$  and  $S$ . The third equation is for the infected weaned pigs. Animals enter this class from the previous one, via contagion, and exit by natural mortality. Note that the data collected on which the birth rate parameter is calibrated already discount possible deaths. Therefore they represent a net birth rate, so there is no need to add here an extra disease-related mortality.

The fourth equation describes the sound weaned pigs, born two months in advance. Here animals can leave by death, but also by being vaccinated, at rate  $k = 0.03$ . This value has been so chosen on the basis of experience, namely the good results it gives. In this last case the weaned pigs enter the class of vaccinated weaned pigs. The latter is described in the seventh equation, into which also enter weaned pigs from the fifth equation, for whom vaccination has been successful. The latter equation describes the evolution of susceptible weaned pigs, which can leave also by contracting either directly or by biohazards the disease, at respective rates  $\eta$  and  $S$ . The sixth equation contains the infected weaned pigs dynamics; in it come the animals leaving from the fifth equation via the two ways of contagion. Note that the pigs in this class are vaccinated as all the animals in the farm are. But for the individuals in this class the vaccination has not been effective, for whatever reason. In other words, the vaccination rate  $k$  mentioned above is to be understood rather to represent the successful rate of vaccination.

The initial conditions of class I are the final values of the newborns coming from the farrowing unit. Also, the initial condition of class II is represented by the final values of weaned pigs in class I, clearly with the value of vaccinated animals initially set to zero. Furthermore, since at about the end of the third month the maternal immunity ends, when the weaned pigs leave class II, becoming fattening pigs, the subdivision between immune and susceptible animals has no further meaning. Therefore both immune and susceptible pigs at the end of the weaning in class II will merge into susceptible fattening pigs.

## 5.2 The fattening unit

We finally model the fattening unit of the farm. It contains pigs from their 4th up to the 9th month of life. Again we subdivided the unit in several classes. After weaning, an animal goes through all the six classes, from I to VI, remaining in each of them for a month. At the end of the sixth fattening month, when the animal is at least 9 months old, it is slaughtered. At this time indeed it reaches the prescribed weight established by the certification procedures for the production of raw ham. In addition, in class II and IV, i.e. at about the fifth and seventh month of age, the animals are vaccinated again, but this renewed vaccinations will be effective only if the former ones had been performed well and they were successful.

In order to better simulate the system, since not all the initial conditions for the fattening class are not known, in what follows these are marked with question marks, in practice they have been chosen as the final outcomes of a previously run one year long simulation, which in turn started from arbitrarily chosen initial conditions. By running the simulation for a whole year, we considered that the arbitrary choice of the initial conditions would in this way be smoothed out. The results of this simulation confirm the goodness of the assumptions and of the general strategy.

Let  $Y = \sum_{i=1}^{20} y_i$ . The equations for the three-months old pigs entering this unit are then

$$\begin{aligned}\frac{dy_1}{dt} &= -ny_1 - Qy_1 - \xi y_1 \frac{1}{Y}(y_2 + y_5 + y_9 + y_{12} + y_{16} + y_{19}); \\ \frac{dy_2}{dt} &= -ny_2 + Qy_1 + \xi y_1 \frac{1}{Y}(y_2 + y_5 + y_9 + y_{12} + y_{16} + y_{19}); \\ \frac{dy_3}{dt} &= -ny_3;\end{aligned}$$

for the four-months old ones

$$\begin{aligned}\frac{dy_4}{dt} &= -ny_4 - Qy_4 - \xi y_4 \frac{1}{Y}(y_2 + y_5 + y_9 + y_{12} + y_{16} + y_{19}); \\ \frac{dy_5}{dt} &= -ny_5 + Qy_4 + \xi y_4 \frac{1}{Y}(y_2 + y_5 + y_9 + y_{12} + y_{16} + y_{19}); \\ \frac{dy_6}{dt} &= -ny_6 - Ky_6; \\ \frac{dy_7}{dt} &= -ny_7 + Ky_6;\end{aligned}$$

for the fifth-months old ones

$$\begin{aligned}\frac{dy_8}{dt} &= -ny_8 - Qy_8 - \xi y_8 \frac{1}{Y}(y_2 + y_5 + y_9 + y_{12} + y_{16} + y_{19}); \\ \frac{dy_9}{dt} &= -ny_9 + Qy_8 + \xi y_8 \frac{1}{Y}(y_2 + y_5 + y_9 + y_{12} + y_{16} + y_{19}); \\ \frac{dy_{10}}{dt} &= -ny_{10};\end{aligned}$$

for the six-months old ones

$$\begin{aligned}\frac{dy_{11}}{dt} &= -ny_{11} - Qy_{11} - \xi y_{11} \frac{1}{Y}(y_2 + y_5 + y_9 + y_{12} + y_{16} + y_{19}); \\ \frac{dy_{12}}{dt} &= -ny_{12} + Qy_{11} + \xi y_{11} \frac{1}{Y}(y_2 + y_5 + y_9 + y_{12} + y_{16} + y_{19}); \\ \frac{dy_{13}}{dt} &= -ny_{13} - Ky_{13}; \\ \frac{dy_{14}}{dt} &= -ny_{14} + Ky_{13};\end{aligned}$$

for the seven-months old ones

$$\begin{aligned}\frac{dy_{15}}{dt} &= -ny_{15} - Qy_{15} - \xi y_{15} \frac{1}{Y}(y_2 + y_5 + y_9 + y_{12} + y_{16} + y_{19}); \\ \frac{dy_{16}}{dt} &= -ny_{16} + Qy_{15} + \xi y_{15} \frac{1}{Y}(y_2 + y_5 + y_9 + y_{12} + y_{16} + y_{19}); \\ \frac{dy_{17}}{dt} &= -ny_{17};\end{aligned}$$

and finally for the eighth-months old ones

$$\begin{aligned}\frac{dy_{18}}{dt} &= -ny_{18} - Qy_{18} - \xi y_{18} \frac{1}{Y} (y_2 + y_5 + y_9 + y_{12} + y_{16} + y_{19}); \\ \frac{dy_{19}}{dt} &= -ny_{19} + Qy_{18} + \xi y_{18} \frac{1}{Y} (y_2 + y_5 + y_9 + y_{12} + y_{16} + y_{19}); \\ \frac{dy_{20}}{dt} &= -ny_{20};\end{aligned}$$

The initial conditions for the susceptible animals are for  $k \in \{4, 11, 18\}$  and for  $i \in \{8, 15\}$

$$y_1(nT^+) = w_4(nT^-) + w_5(nT^-), \quad y_k(nT^+) = y_{k-3}(nT^-), \quad y_i(nT^+) = y_{i-4}(nT^-);$$

those for the infected are for  $k \in \{5, 12, 19\}$  and for  $i \in \{9, 16\}$

$$y_2(nT^+) = w_6(nT^-), \quad y_k(nT^+) = y_{k-3}(nT^-), \quad y_i(nT^+) = y_{i-4}(nT^-);$$

for the properly vaccinated animals we have for  $k \in \{10, 17, 20\}$

$$y_3(nT^+) = w_7(nT^-), \quad y_k(nT^+) = y_{k-3}(nT^-);$$

and finally for the vaccinated ones for which renewed vaccinations occur, we have

$$y_6(nT^+) = y_3(nT^-), \quad y_{13}(nT^+) = y_{10}(nT^-), \quad y_7(nT^+) = 0, \quad y_{14}(nT^+) = 0.$$

The equations for  $y_1, y_4, y_8, y_{11}, y_{15}$  and  $y_{18}$  describe the susceptible fattening pigs. They exit these classes via mortality at rate  $n$ , and by becoming infected through biohazard at rate  $Q$  or via direct contact, at rate  $\xi$ . The variables  $y_2, y_5, y_9, y_{12}, y_{16}$  and  $y_{19}$  denote the infected animals, which can die at rate  $n$ , and enter these classes by becoming infected, i.e. from the corresponding former classes. The equations for  $y_3, y_{10}, y_{17}$  and  $y_{20}$  stand for the properly vaccinated animals, in which the vaccination has been effective;  $y_6$  and  $y_{13}$  are as the former ones, but in addition since they describe the classes in which the renewed vaccinations occur, they are characterized by terms containing the vaccination rate  $K$  that we take to be the same as for the weaning unit,  $K = k$ . If the vaccination is successful, the animal migrates into the pigs subjected to booster vaccination class,  $y_7$  and  $y_{14}$ , simply denoted by booster in what follows.

From the four classes, susceptible, infected, well vaccinated and booster pigs, the animals migrate, in the following month, to only three possible classes of susceptible, infected and well vaccinated pigs, since the susceptible pigs will contain the previous susceptible animals and the leftovers of the well vaccinated ones, i.e. those animals for which the third vaccination has not been successful, so that their immunization is being lost as time goes by. The new well vaccinated class at this time will contain the former booster.

Finally the seventh and fourteenth equations describe the booster, and contain the populations leaving from equations 6 and 13 at rate  $K$ .

## 6 Simulations

We now illustrate the performed simulations. We tried first of all to analyze the relationship between biohazards and the presence of infection in the two reproduction units, namely the gestation and farrowing units. Then we considered infection in the fattening units. Finally we looked at possible scenarios when the vaccination is badly implemented.

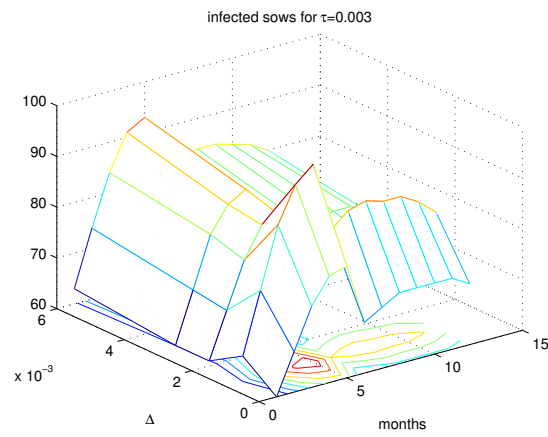
We report the simulations results in summarizing Figures.

### 6.1 Infection in gestation and farrowing units

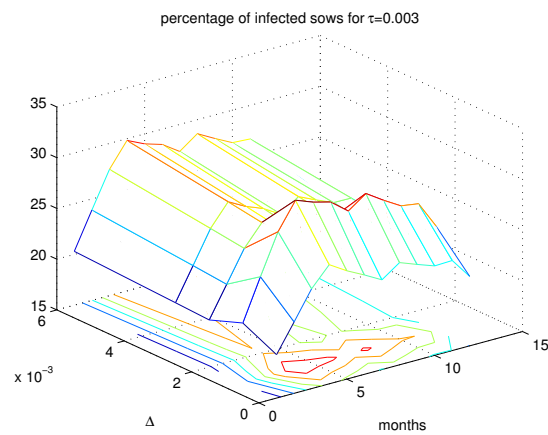
Fix  $\alpha = 0.006$ ,  $\beta = 0.002$ ,  $\gamma = 0.004$ .



**Fig. 4** Infected weaned pigs evolution during a whole year. Here we fix the value of external contamination rate at  $\tau = 0.003$ .

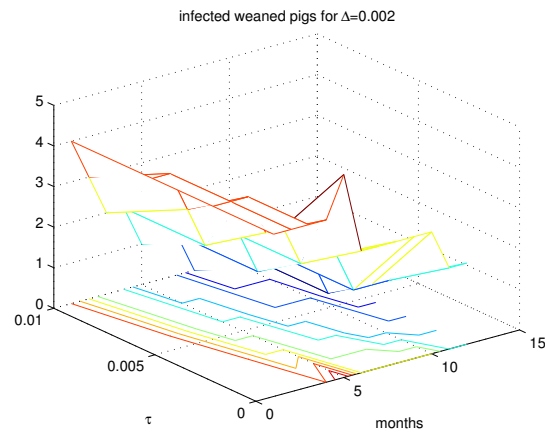


**Fig. 5** Infected sows evolution during a whole year. Here we fix the value of external contamination rate at  $\tau = 0.003$ .

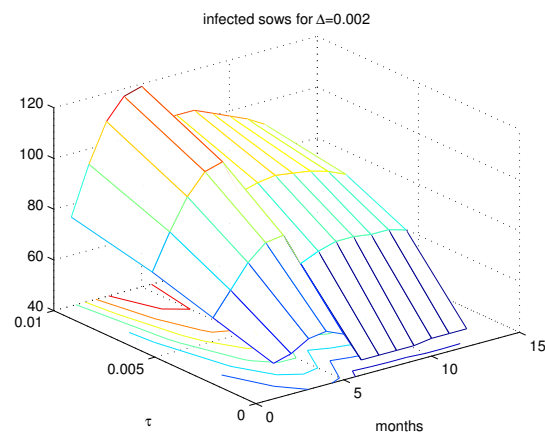


**Fig. 6** Percentage of infected sows evolution during a whole year. Here we fix the value of external contamination rate at  $\tau = 0.003$ .

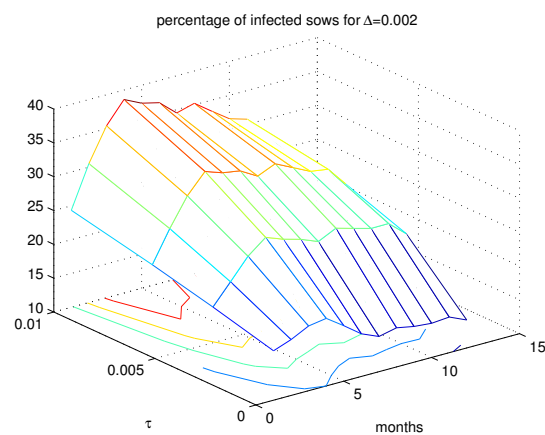




**Fig. 7** Infected weaned pigs evolution during a whole year. Here we fix the value of biohazard rate at  $\Delta = 0.002$ .



**Fig. 8** Infected sows evolution during a whole year. Here we fix the value of biohazard rate at  $\Delta = 0.002$ .



**Fig. 9** Percentage of infected sows evolution during a whole year. Here we fix the value of biohazard rate at  $\Delta = 0.002$ .

To better analyze the results, for each simulation we report in the following table the total number of infected newborns and the percentage of infected sows, in the whole year, for the two reproductive units, gestation and farrowing units: these are the averages of the percentage of infected sows in each month of the year.

In the absence of external contamination and biohazards, we have respectively the average number of infected weaned pigs as 2.244, and the percentage of infected shows at 14.44.

simulation $\tau = 0.003$	# infected weaned pigs	average % infected sows
Reference: $\Delta = 0, \tau = 0$	2.244	14.44
C: $\Delta = 0$	2.3667	23.86
H: $\Delta = 0.001$	101.6042	28.15
A: $\Delta = 0.002$	28.324	24.91
F: $\Delta = 0.003$	39.947	25.39
G: $\Delta = 0.006$	70.1768	26.69
simulation $\Delta = 0.002$	# infected weaned pigs	average % infected sows
Reference: $\Delta = 0, \tau = 0$	2.244	14.44
I: $\tau = 0$	40.4711	16.70
A: $\tau = 0.003$	28.324	24.91
D: $\tau = 0.006$	21.1276	29.51
E: $\tau = 0.01$	15.5476	32.98

We now analyze the relationship between biohazard values in the two units, i.e.  $\tau$  in the gestation unit and  $\Delta$  in the farrowing unit, and the percentage of infected sows.

We take simulation *A* as reference because it is the common simulation to both cases that includes both biohazards and external contamination.

Taking a varying value for  $\Delta$  from 0.002, for simulations *C*, *F*, *G* and *H*, we have for  $\Delta = 0$  the value of infected sows 23.86%, for  $\Delta = 0.003$  the value 25.39%, for  $\Delta = 0.006$  the value 26.69% and for  $\Delta = 0.01$  the value 28.15%.

We can therefore conclude that in order to decrease the number of infected sows, it is not convenient to act excessively on containing the biohazard  $\Delta$ : since to ensure total biosafety has very high costs, the benefit one obtains in such case is not so much relevant. The ease with which one goes from 24.91% up to almost 29% for  $\Delta = 0.01$  shows however that it is not wise to disregard  $\Delta$ . Its increase in fact leads to observable changes.

When  $\tau$  varies from 0.003, in simulations *D*, *E* and *I*, we find for  $\tau = 0.006$  the value 29.51%, for  $\tau = 0.01$  the value 32.98% and for  $\tau = 0$  the value 16.70%. Thus,  $\tau$  is much more relevant. Its growth leads to large percentage increases of the infected sows, but if we can minimize it, also a considerable reduction in the infected animals will be achieved, in some cases they drop even below 17%.

Finally, by minimizing both biohazard parameters, simulation *B*, we reach the value 14.44%, which is not so far from the threshold one can achieve by acting just upon  $\tau$ .

We now analyze the relationship between the biohazard parameters and the number of infected weaned pigs which are introduced into the weaning unit and later on into the fattening unit, in the whole year, taking always as reference simulation *A*.

As  $\Delta$  varies from the value 0.002, simulations *C*, *F*, *G* and *H*, for  $\Delta = 0$  the value 2.3667 is obtained, for  $\Delta = 0.003$  the value 39.947, for  $\Delta = 0.006$  the value 70.1768 and for  $\Delta = 0.01$  the value 101.6042.

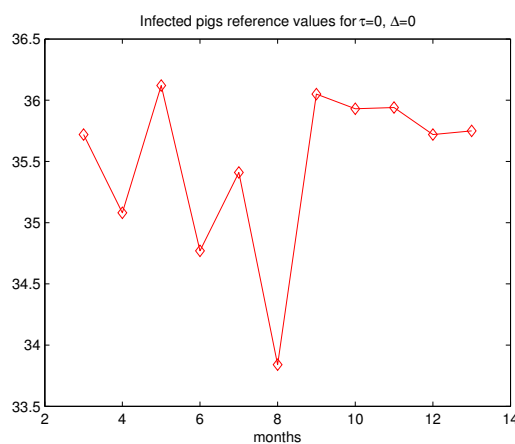
Thus, the role played by  $\Delta$  is relevant: by minimizing it, we can practically extinguish the disease from the weaned pigs, while if it is left unchecked, the infected animals grow unboundedly.

As  $\tau$  varies from 0.003 in simulations *D*, *E* and *I*, we find for  $\tau = 0.006$  the value 21.1276, for  $\tau = 0.01$  the value 15.5476 and for  $\tau = 0$  the value 40.4711.

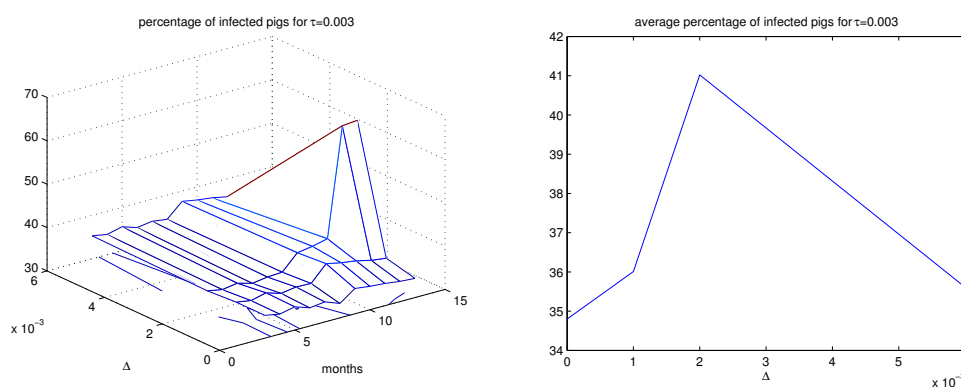
If both biohazard parameters are minimized, simulation  $B$ , we find the minimum value 2.244%. This is smaller, even though just by a little, to the threshold found for  $\Delta = 0$ . Thus biosafety in the farrowing unit is absolute, the contagion probability for newborns is so small that to get the disease for the newborns without maternal immunity, i.e. coming from susceptible mothers, when also  $\tau = 0$  is smaller than the advantage we have given by the smaller number of infected sows coming from the gestation unit. Since however to reach total biosafety in at least one of the two environments in practice it is impossible, and in view of the fact that to have  $\tau = \Delta = 0$  entails little improvement over the situation for  $\Delta = 0$ , it seems therefore preferable not to exceed in biosafety in the gestation unit, until we are sure to have achieved a very high biosafety standard in the farrowing unit, and to maintain it in time.

## 6.2 Infection in the fattening unit

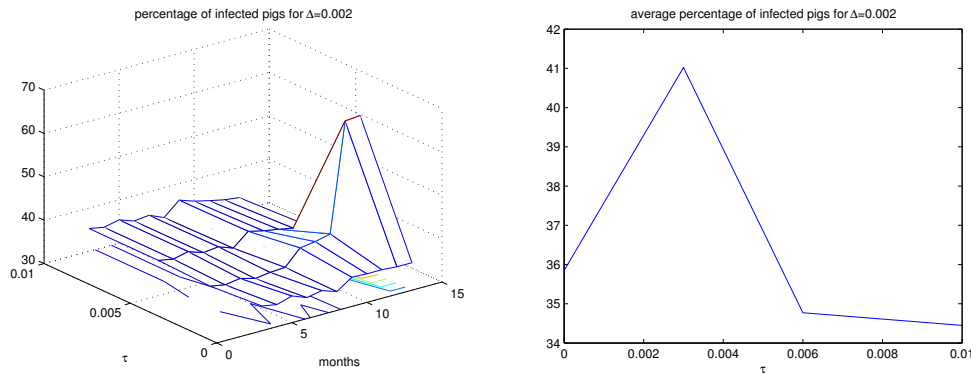
We want now to analyze the situation in the fattening unit. We observe how the number of infected animals to be sent to slaughter changes as a function of the biosafety in the two units, gestation and farrowing units. Indeed these are the two parameters on which it is easier to operate in practice. All the remaining parameters have the same values in all the simulations reported in the next tables.



**Fig. 10** Reference values in the fattening unit for no external contamination rate and biohazards,  $\tau = 0$ ,  $\Delta = 0$ , with an average value of 35.48%.



**Fig. 11** Left: Percentage of infected pigs evolution in the fattening unit. Here we fix the value of external contamination rate at  $\tau = 0.003$ . Right: Averages in time as function of  $\Delta$  of the percentage of infected pigs evolution in the fattening unit. Here we fix the value of external contamination rate at  $\tau = 0.003$ .



**Fig. 12** Left: Percentage of infected pigs evolution in the fattening unit. Here we fix the value of biohazard rate at  $\Delta = 0.002$ . Right: Averages in time as function of  $\tau$  of the percentage of infected pigs evolution in the fattening unit. Here we fix the value of biohazard rate at  $\Delta = 0.002$ .

The previous data show how by improving biosafety in gestation and farrowing units it is not possible to reduce the average percentage of infected animals in the fattening unit, below a threshold of about 35%. When  $\tau = 0$  in simulation *I*, we find 35.85%, for  $\Delta = 0$ , simulation *C*, we have 34.80%. Even by decreasing biosafety things do not improve much, since by increasing  $\Delta$  to 0.006, simulation *G*, we find the value 35.61% and for 0.01, simulation *H* we have 36.01%. By increasing  $\tau$  to 0.006, simulation *D*, we arrive at 34.77% and for  $\tau = 0.01$ , simulation *E*, we get the value 34.45%.

By setting finally  $\tau = \Delta = 0$ , simulation *B*, we find the value 35.48%.

From these data, we find that the best way of modifying biosafety is to allow a slight increase in the biohazard in the farrowing unit followed by a reduction of  $\Delta$ . Improving both parameters does not lead to satisfactory results.

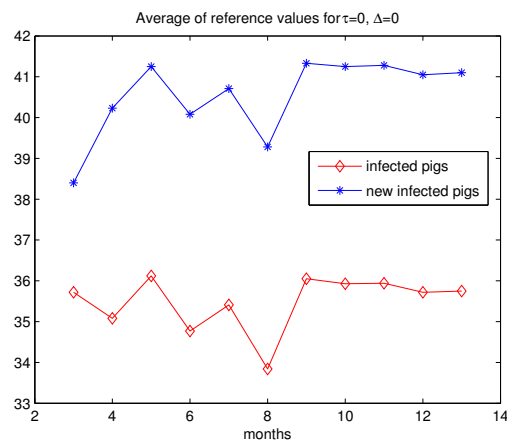
Looking at the percentages, in the various simulations we find once again the previous considerations, but we also remark the large increase of infected percentages in simulation *A*. In it we arrive at 64.75% for  $t = 390$ . From this, the importance of keeping well below certain thresholds both biohazard rates is clear, in order to avoid a sudden increase in the infected animals in the fattening unit.

In conclusion it does not seem possible to eradicate the disease from the entire farm, just by acting on the gestation and farrowing units. However by improving their biosafety it is possible to reduce significantly the number of infected in the same units, and to contain them in the fattening unit. It remains to assess how to reduce biohazard in the first two units when the disease is present in the fattening unit, since the epidemic spreads not only by direct contact but also via other means, and the closer one animal is to an affected area, the higher the possibility of getting the infection. But these considerations are beyond the scope of this model, since they require to work with biohazard parameters which are directly related to the number of infect animals present in the vicinity of each unit in the farm.

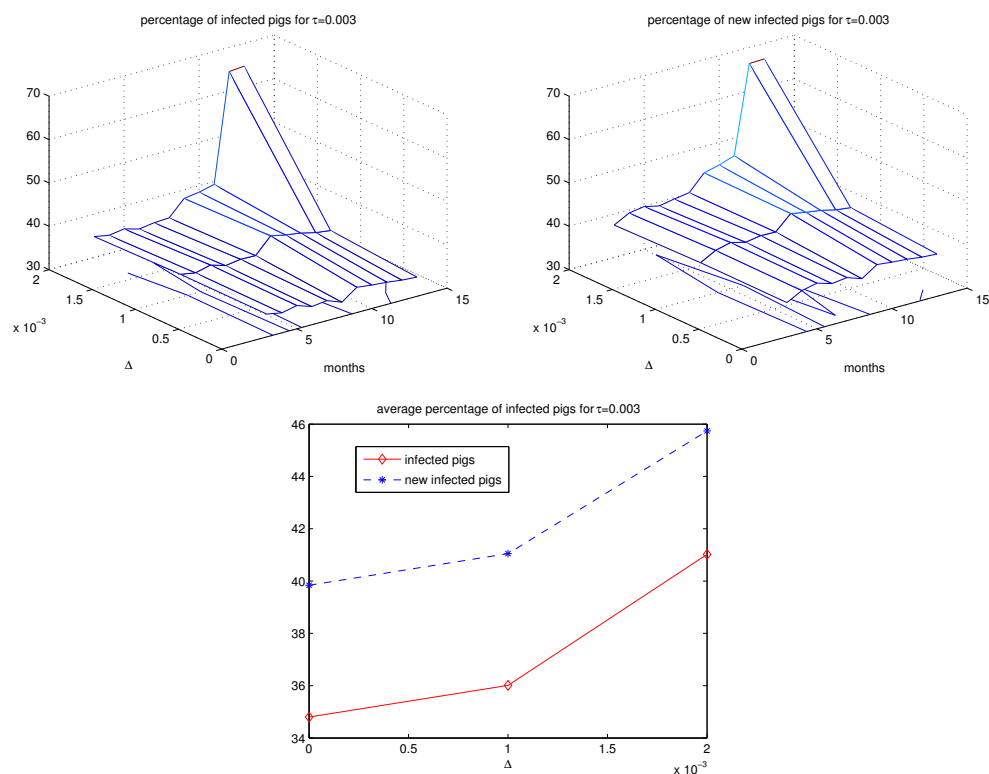
### 6.3 Scenarios for bad implementation of vaccination

Since one of the main problems arisen during the implementation of the “Piano Nazionale di Controllo della Malattia di Aujeszky” (National Control Plan for the AD) was the omission or the bad execution of the third vaccination, which should be done between the sixth and the seventh month of age, we finally ran further simulations to assess its impact on the disease eradication plan.

We summarize in the tables some of the simulations already discussed above for the analysis of the infected percentages in the fattening unit. Aside of the “infected percentage” column, under the heading “new infected percentage” are the values of the same simulations, performed however under the assumption that the third vaccination is not performed.

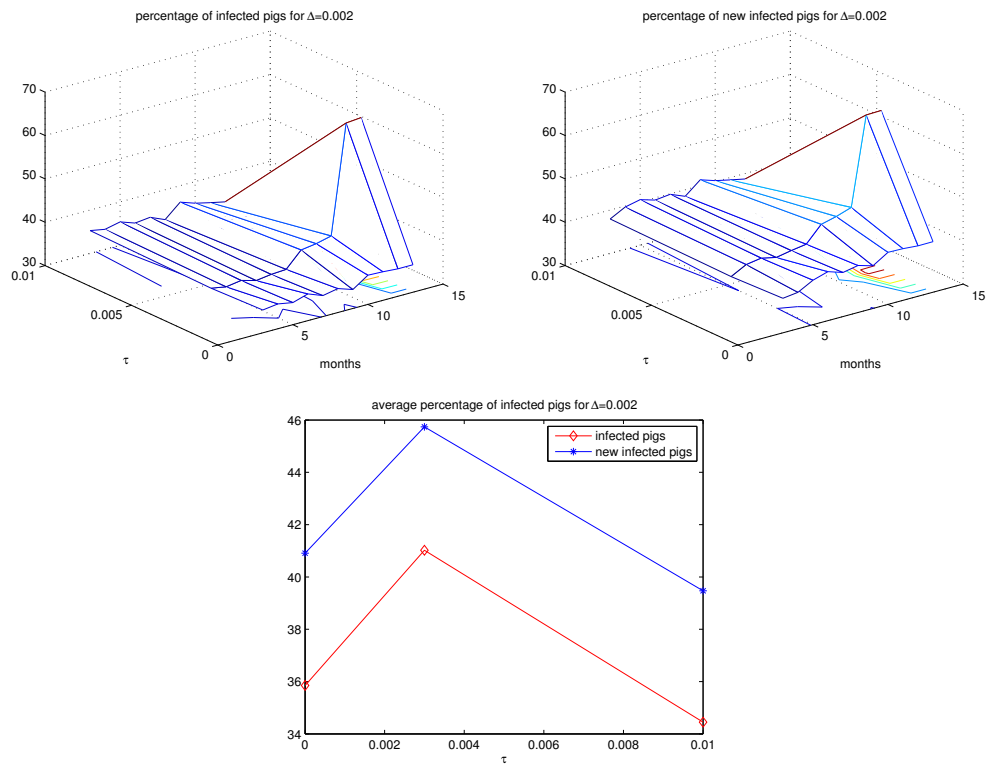


**Fig. 13** Reference values in case of bad implementation of the vaccine for no external contamination rate and biohazards,  $\tau = 0, \Delta = 0$ , with an average value of 35.48%.



**Fig. 14** Top. Left: Percentage of infected pigs evolution in case of bad implementation of the vaccine. Here we fix the value of external contamination rate at  $\tau = 0.003$ . Right: The same figure for new infected pigs. Bottom. Averages in time as function of  $\Delta$  of the percentage of infected pigs evolution in case of bad implementation of the vaccine. Here we fix the value of external contamination rate at  $\tau = 0.003$ .

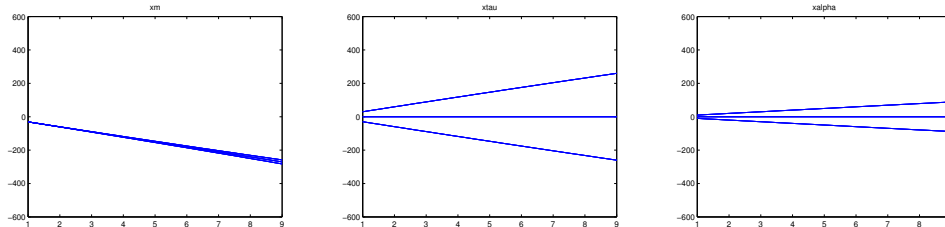




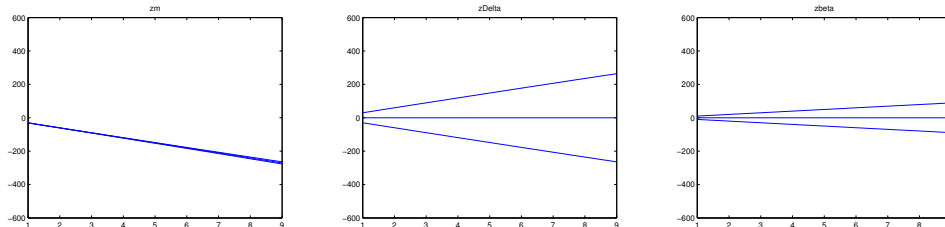
**Fig. 15** Top. Left: Percentage of infected pigs evolution in case of bad implementation of the vaccine. Here we fix the value of biohazard rate at  $\Delta = 0.002$ . Right: The same figure for new infected pigs. Bottom. Averages in time as function of  $\tau$  of the percentage of infected pigs evolution in case of bad implementation of the vaccine. Here we fix the value of biohazard rate at  $\Delta = 0.002$ .

From all the simulations it is clear that if the third vaccination is not performed, the percentage of infected animals increases of about 5%.

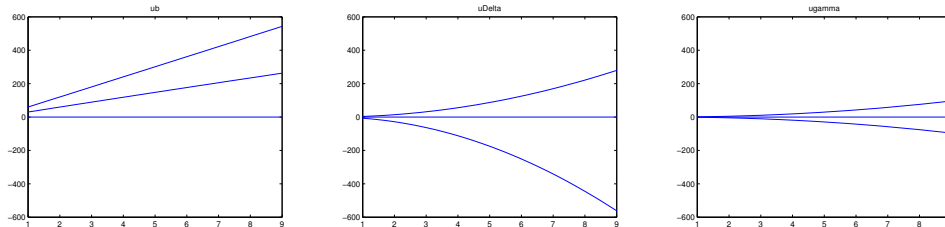
#### 6.4 Sensitivity



**Fig. 16** Sensitivity of  $x$  with respect (left to right) the parameters  $m$ ,  $\tau$  and  $\alpha$ .



**Fig. 17** Sensitivity of  $z$  with respect (left to right) the parameters  $m$ ,  $\Delta$  and  $\beta$ .

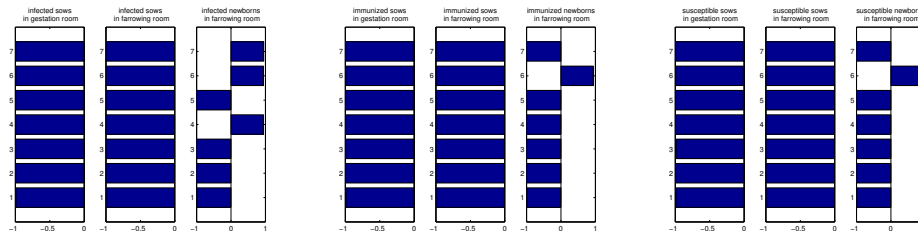


**Fig. 18** Sensitivity of  $u$  with respect (left to right) the parameters  $b$ ,  $\Delta$  and  $\gamma$ .

Finally, we have run a sensitivity analysis on the model to assess what are the parameters which changing affect the system more. The results are shown in Figures 16, 17 and 18 respectively for the variables  $x$ ,  $z$  and  $u$ . To allow a better comparison, the vertical scale has been kept the same in all figures, namely the interval  $[-600, 600]$ . Clearly the most sensitive quantity is represented by the newborns  $u$ , which heavily depend on the birth rate  $b$  and on the horizontal disease transmission rate  $\Delta$ . Secondly, we find that the sow populations are influenced in a very similar way by a couple of parameters: namely, the sows in the gestation unit  $x$  by the external contamination, modeled by parameter  $\tau$  and those in the farrowing unit  $z$  once again by the parameter  $\Delta$ ; in a similar way to this one, they are also both influenced by mortality  $m$ . Next, the three populations depend less markedly on the last parameter, the three horizontal transmission rates, namely  $\alpha$  for  $x$ ,  $\beta$  for  $z$  and  $\gamma$  for  $u$ .

We also calculated the correlation among the parameters relative to the gestation and farrowing units and their populations, Figure 19. The parameters considered are, in the bottom-up order of the figure,  $m$ ,  $\alpha$ ,  $\tau$ ,  $\Delta$ ,  $\beta$ ,  $b$ ,  $\gamma$ . The infected sows in both units appear to be negatively correlated with all these parameters. Instead,

the newborns appear to be positively correlated with  $\Delta$ ,  $b$  and  $\gamma$ , respectively the contamination due to external factors, the net birthrate and the contact rate, all these apparently at the same level. All the immunized animals are negatively correlated with all the parameters with the exception of the newborns, that appear to be influenced by their birthrate, a fact which is quite plausible. The same behavior is exhibited by the three susceptible populations. In fact the correlation coefficients in the two cases differ, but only the least significant digits.



**Fig. 19** Correlations between the system's parameters and the infected (left), immunized (center) and susceptible (right) populations in the gestation and farrowing units. The parameters, bottom to top, are the following ones:  $m$ ,  $\alpha$ ,  $\tau$ ,  $\Delta$ ,  $\beta$ ,  $b$ ,  $\gamma$ . In each frame, the left column contains the results relative to the sows in the gestation room, the central one the sows in the farrowing unit and the right one the newborns in the farrowing unit.

## 7 Conclusions

The various simulations show that even by sensibly improving the biosafety in the gestation and farrowing units, it is not possible to reduce the average prevalence of the disease in the fattening unit of the farm, below a critical threshold of about 35%. The best option in this sense appears to avail a larger biohazard in the gestation unit, but followed by a stricter reduction of biohazards in the farrowing unit. In fact, this guarantees a better acquired immunity for the newborns. To improve instead biosafety in both environments does not lead to satisfactory results. It is useless to improve biosafety in the gestation unit until it is not possible to ensure and maintain in time a very elevated biosafety standard in the farrowing unit.

From our simulations it is possible to identify some necessary thresholds for biosafety in both gestation and farrowing units, in order to avoid a sudden jump in the number of infected in the fattening unit. It does not seem however possible to eradicate the disease from the entire farm, by acting only on the gestation and farrowing unit. However, by taking measures to improve on their biosafety it is possible to perceivably reduce their number of infected and to bound the infected in the fattening unit. It also seems to be difficult to reduce biohazards in the gestation and farrowing unit when the disease is present in the fattening unit, since the epidemics can spread not only by direct contact, but also via other indirect methods, and the better it spreads the closer animals are to infected farming areas. Further, since the last vaccination very often is neglected by farmers, in view of the fact that animals at that age are near their slaughtering time, we performed some simulations to ascertain the impact of this omission. By comparing the results in the case of the complete cycle of three vaccinations and the one in which the farmer omits the last one, in all the simulations it appears that neglecting the final vaccination leads to an increase of the infected of about 5%.

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