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# ▶ To cite this version:

Vianney Sicard, Sébastien Picault, Mathieu Andraud. Coupling spatial and temporal structure in batch rearing modeling for understanding the spread of the swine influenza A virus. Annual Conference of the Society for Veterinary Epidemiology and Preventive Medicine (SVEPM), Mar 2022, Belfast (Northern Ireland), Ireland. pp.177-187. hal-03790020

HAL Id: hal-03790020 https://hal.inrae.fr/hal-03790020

Submitted on 30 Nov 2022

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# COUPLING SPATIAL AND TEMPORAL STRUCTURE IN BATCH REARING MODELLING FOR UNDERSTANDING THE SPREAD OF THE SWINE INFLUENZA A VIRUS

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### **SUMMARY**

The ability to identify through modelling the main routes of pathogen spread, the best herd management practices and associated control measures is a key step to improve livestock health. We developed a new AI-based approach to account for the coupling between social and spatial structuring at different levels in pig herds, and demonstrated its added value to propose and assess effective and realistic control measures on swine influenza A virus.

# INTRODUCTION

Swine influenza A viruses are widely spreading in pig production units (Salvesen and Whitelaw, 2021). In conjunction with other pathogens, they are recognized as a main etiological agent responsible of the porcine respiratory disease complex (PRDC), with high economic impact for pig producers (Fablet et al., 2012; Woeste, K., 2007). Like most RNA viruses, SwIAVs are rapidly evolving and are of primary concerns regarding both animal and human health, due to the potential emergence of zoonotic viral strains (Deblanc et al., 2020).

Contrary to the expected behaviour in epidemic forms, SwIAVs has been shown to remain endemic in herds, inducing successive and regular waves in batches of growing pigs with possible co-circulation of different virus strains, favouring reassortments (Chastagner et al.,

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2019; Rose, 2014). This endemic situation was found to be associated with the partial protection provided by maternally derived antibodies (MDAs), slowing down the batch-level transmission process and favouring the interaction of infectious piglets with the subsequent batches (Cador et al., 2016a). Another pivotal factor is the transfer of infectious particles between the different sectors, either by airborne route or due to management constraints, e.g. movements of animals between the barns (Fablet et al., 2013).

Mathematical modelling approaches have been developed to tackle SwIAV infection dynamics on farms. For this purpose, transmission parameters have been estimated from experimental data to ascertain the role of specific factors affecting the transmission dynamics, *e.g.* MDAs (Allerson et al., 2013; Cador et al., 2016b) or vaccine-induced immunity (Romagosa et al., 2011). In turn, these parameters have been used to feed dynamic models representing specific farming systems. These models were based on MSIR principles representing the evolution of the population through the different epidemiological states, and on metapopulation approaches, with subgroups corresponding to breeding herds and growing pigs respectively. However, when farrow-to-finish pig herds were represented in Europe (Cador et al., 2017; Pitzer et al., 2016), only the breeding herd and their progeny up to weaning-age were considered in the US (White et al., 2017), limiting so the interaction of non-contemporary piglets.

To go further in the understanding of the impact of batch management and housing on the spread of SwIAV at different scales, and identify possible realistic levers, new modelling approaches had to be developed to overcome the complexity of implementing reliable, revisable and flexible simulation code. This was made possible through the development of artificial intelligence methods, which led to a new epidemiological modelling software, EMULSION (Picault et al., 2019). We extended EMULSION to incorporate highly structured populations such as those found in pig farm management (Sicard et al., 2021), which makes possible to model a realistic farrow-to-finish pig farm.

As a proof of concept to highlight the added value of accounting for highly structured populations in epidemiological models and the interest of providing generic methods to do so, we reimplemented a simple model from the literature (White et al., 2017), consisting of two barns (gestation and farrowing), in the extended EMULSION software. We kept all original epidemiological parameter values and adapted housing and farming practices to reflect realistic farrow-to-finish French farms, including post-weaning and fattening barns. The model was then extended to represent the infection dynamics in a typical farrow-to-finish pig farm, keeping the epidemiological assumptions unchanged.

We highlight the main outcomes of this explicit representation of spatiality and batch management on SwIAV spread and finally discuss possible applications of this approach to difficult questions in livestock epidemiology.

### MATERIALS AND METHODS

# Organizational model

§ To model the SwIAV pathosystem in the complex batch management system, we used the epidemiological mechanistic modelling framework EMULSION (Picault et al., 2019) extende with a new organizational multi-level agent-based system (Sicard et al., 2021). This original approach makes it possible to represent both the complexity of herd management, and the multi-level aspect of the spatial and social structuring of the population with modularity and flexibility. More specifically, we introduced two organizations. The first one represented a realistic batch management based on existing timetables. The second one represented the multi-level spatial partition of the environment, composed of sectors subdivided into rooms. It was possible to amend the model without additional code and to easily explore different hypotheses regarding these structures and their epidemiological connections.

# § Batch management

Sows and piglets were seen as two sub-populations, structured and managed by the producer. Batch farrowing herd management was considered with all-in-all-out management procedures.

- § Physiological stage: the animals evolve through different physiological statuses according to their type (sow or piglet), and their physiological status evolution: insemination, gestating and lactating stages for sows, and suckling, post-weaning and fattening stages for piglets. Therefore, sows and piglets shared only one common environment during lactation/suckling period up to weaning which occurred at 3 or 4 weeks of age. After fattening, piglets leaved the system to be taken to the slaughterhouse (Sicard et al., 2021).
- <u>Batches:</u> piglets and sows are bred in batches, to guarantee a homogeneous evolution of the physiological stages. Batches are designed to be and remain consistent, i.e. that all animals are in the same physiological stage at the same time, according to their type (sow or piglet). In the model, we considered a management in 7 batches with an interval of 21 days (Sicard et al., 2021).

<u>Housing:</u> the farm was divided into sectors corresponding to specific physiological stages (Fig. 1). Thus, 5 sectors were considered: the mating, gestating, farrowing, post-weaning and

fattening sector. Each sector was divided into rooms, and each room could only host one batch at a time (all-in-all-out management), batches being assigned to a room depending on availability. The number of rooms in a sector was set out according to the number of batches in a sector at the same time (Table 1).

	Mating sector	Gestating sector	Maternity sector	Post- weaning sector	Fattening sector
Physiological stage	Inseminatio n	Gestating	Suckling	Post- weaning	Fattening
Number of batches to be housed	2	4	2	3	6
Sector occupancy (days)	35	77	28	or	or

Table 1

# **SwIAV** transmission

MSEIR model: we developed an individual-based, discret-time stochastic model. Five health states were modelled: maternal immunity (M), susceptible (S), exposed (E), infectious (I), and recovered (R). Recoverd/Immune sows deliver maternally derived antibodies (MDAs) to their piglets. However, the protection conferred to piglets is only partial (Allerson et al., 2013; Cador et al., 2016b; White et al., 2017) and they were assumed to be potentially infected though having lower susceptibility to infection. As described in (White et al., 2017), susceptible and exposed sows gave birth to piglets without maternal immunity, whereas infected and recovered sows gave birth to piglets with maternal immunity. All individuals were assumed susceptible to infection after active immunity waning (MSEIRS)

<u>Direct transmission:</u> it corresponds to transmission from infected animals to susceptible roommates. As in (White et al., 2017), a density-dependant transmission was assumed, due to population size fluctuations through demographics processes.

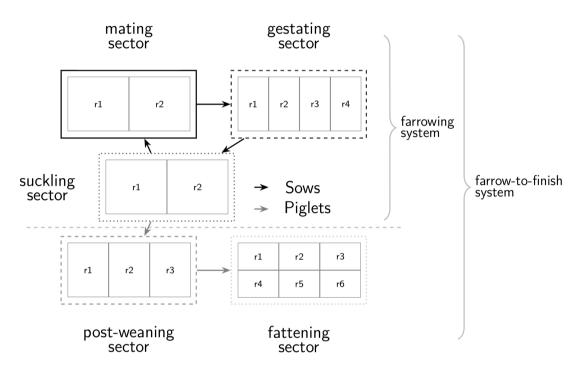


Figure1

<u>Between-room transmission:</u> it corresponds to the transmission between the rooms within a sector. Values varied from (which was equivalent to having no rooms in the sector) to .

<u>Between-sectors transmission:</u> it corresponds to the transmission between buildings through airborne and biosecurity breaches between sectors. The parameter value was modulated depending on the scenarios.

# SwIAV control

Control strategies based on increased biosecurity levels affecting the indirect transmission between rooms and sectors. Each scenario was run on two different farm systems: a farrowing system with a mating, gestating and suckling sector (piglets then leave the system after suckling) and a farrow-to-finish farm.

<u>Reference scenario (Ref):</u> one room per sector and an indirect transmission between sectors was assumed, with baseline value corresponding to the transmission rate in (White et al., 2017) (Table 2).

<u>Full isolation scenario (FI)</u>: it assumed only direct transmission, i.e. no transmission between sectors nor between rooms. In this scenario, we expected the SwIAV to be contained only in batch #1.

<u>Scenarios with partial isolation (PI0-5):</u> we explored a reduction in indirect transmission, e.g. due to better isolation, assuming the same effect both between sectors and between rooms. The parameter values were modulated through a logarithmic scale from to assess their impact.

# Simulation

The simulation were run over 645 days, starting with a burning period of two sow cycles (days) after which the structure of the population reached the observed periodic pattern in the considered farming system, followed by 365 days (one year) after the introduction of the infected sow. Each scenario was iterated 100 times to account for variations caused by model stochasticity. For each simulation, SwIAV was introduced at 280 days in a fully naive herd through an infected sow in batch #1, i.e. at the beginning of the third cycle (insemination stage).

Each animal was identified by its batch membership and its batch farrowing rank (BFR). Thus, we could discriminate piglets which were in fattening from the younger at the same time for the same batch. At the beginning, batch #1 was in BFR #1 and others in BFR #0.

# **RESULTS**

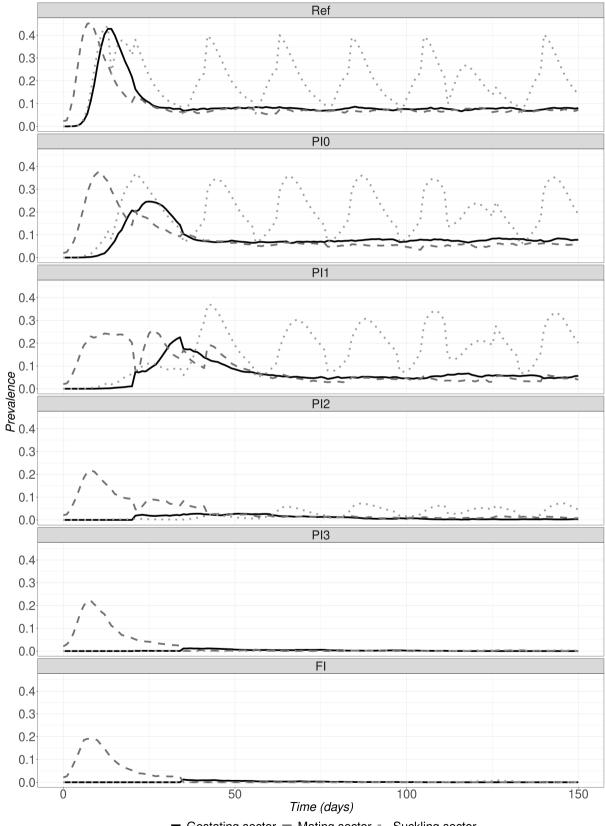
# SwIAV prevalence

Figure 2 shows the prevalence per sector for a farrowing farming system after introducing an infected sow in insemination sector. Scenario Ref, with one room per sector and indirect transmission between sectors, was close to the results obtained by (White et al., 2017): a first peak during the first 25 days and a persistence thereafter. Following scenarios revealed the importance of the farrowing sector, where sows and piglets were mixed, and illustrate the same conclusion about the relevance of isolating the sector containing piglets.

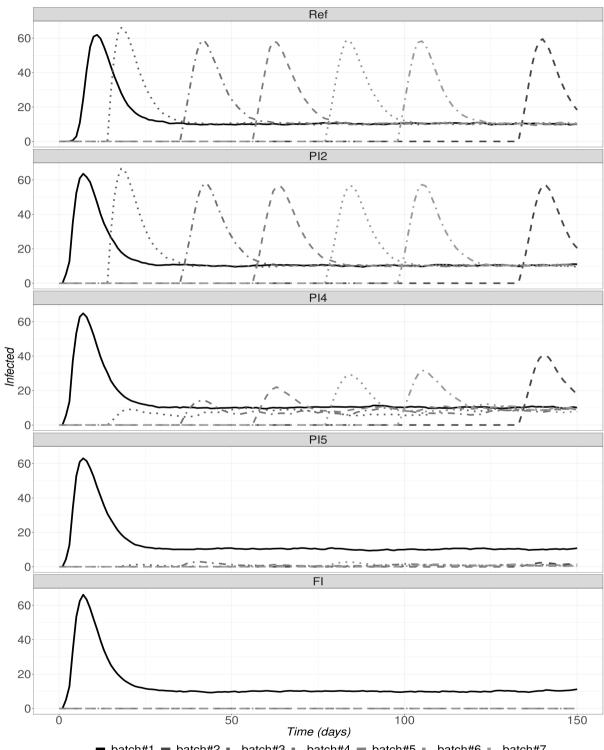
Figure 3 shows the number of infected piglets in BFR #3 by batch after introducing an infected sow in insemination sector for a farrowing-to-finish farming system. By varying  $\beta$  value through log scale, a relevant effect emerged at .

In scenario PI2, the impact was close to the reference scenario, because the factor is almost the same as the value of the indirect transmission parameter, except that the indirect transmission value is also applied for between-room transmission. The impact of control was found substancial when transmission was reduced by (Figure 4 and Figure 5). The results showed that SwIAV persists in the batch #1 for each scenario, due to the length of the immunity period, but that the strong isolation of batches, through measures implemented at sector and room levels, is a key factor in the SwIAV spread control.

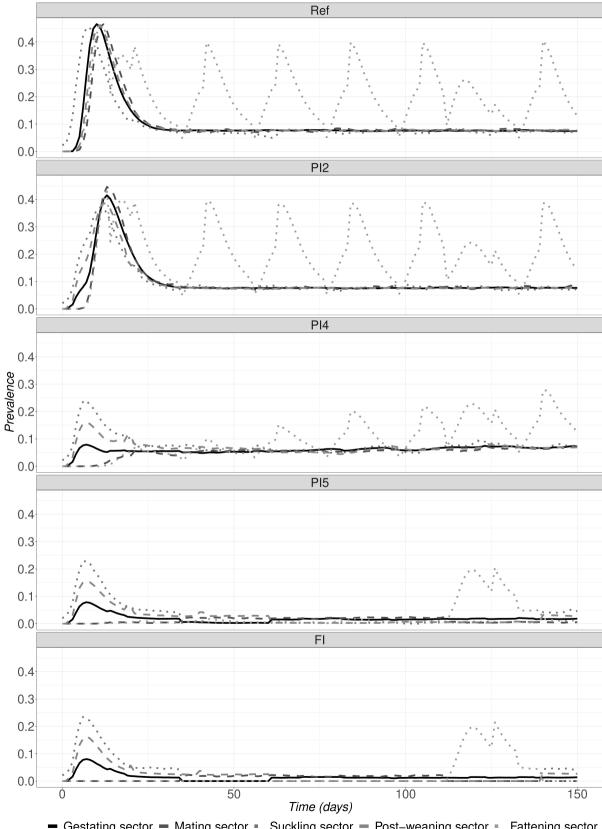
The same effects are observed on Fig. 4 which shows the herd prevalence. Scenario PI4 shows that the infection sets in gradually because of the high contagiousness of SwIAV. Each peak corresponds to piglet farrowing in each batch. The peak observed in each scenario at 120 days, corresponds to piglets farrowing in batch #1.



- Gestating sector - Mating sector - Suckling sector Figure 2



- batch#1 - batch#2 - batch#3 - batch#4 - batch#5 - batch#6 - batch#7 Figure3



ullet Gestating sector ullet Mating sector ullet Suckling sector ullet Post-weaning sector ullet Fattening sector Figure 4

### DISCUSSION

- § EMULSION provides a generic and flexible framework for epidemiological modelling, however it did not take into account highly structured systems (Picault et al., 2019). Therefore, the need to develop a specific solution addressing organizational aspects proved essential. The solution intended to be generic and revisable, based on artificial intelligence, relies on the coupling of multi-level agent-based system and organizational concepts (Sicard et al., 2021). It be applied to several modelling situations. It is thus possible to explicitly represent organizational aspects of the population (social and spatial), with their relationship to environmental spread as encountered in pig farming system with a batch management, as a structured text file which is processed automatically by the simulation engine and can be reviewed or revised at any moment.
- § Other models of SwIAV spread in pig farms had already been developed, yet coming with a high cost regarding model programming, hence difficult to maintain, adapt or revise (Allerson et al., 2013; Cador et al., 2016b; White et al., 2017). In our case, we have made it possible to model structured population in a batch management context while remaining flexible, revisable and reproducible.

We adapted the US farrow-to-finish pig herd model to account the social and spatial organization aspect involved in the French batch management system. With a single model, we could easily switch between farrowing herd and farrow-to-finish herd, and apply different scenarios.

Results demonstrated the major role played by indirect transmission between rooms. Because of the strong force of infection, the control measures to be taken must be really efficient in reducing the airborne transmission between rooms and sectors, with values remaining realistic regarding airborne pathogens (Tellier, 2009). The SwIAV modelling, with organizational aspects, provides a proof of concept of our modelling solution, through its ability to account for multi-level aspects and the highly structured population.

The capacity of the model to take into account organizational aspects of pig herd management by batch, makes it possible to evaluate the impact of different control measures at different scales. One perspective is to assess the impact of coupled control measures applied at different levels details. Furthermore, our modelling methodology is able to take into account deviation in management procedures, or inter-batch piglets transfers, that could be an interesting prospect.

### **ACKNOWLEDGEMENTS**

This work is supported by a grant from INRAE (Animal Health Division) and the Region Pays de la Loire. We are grateful to the INRAE MIGALE bioinformatics facility (MIGALE, INRAE, 2020. Migale bioinformatics Facility, doi: 10.15454/1.5572390655343293E12) for providing computing resources. This work was performed unsing HPC ressources from GENCI-IDRIS (Grant 2021- AP010311702).

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