# Pig herd management and infection transmission dynamics: a challenge for modellers.

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## Abstract

The control of epidemics requires a thorough understanding of the complex interaction between pathogen transmission, disease impact and population dynamics and management. Mechanistic epidemiological modelling is an effective way to address this issue, but handling highly structured and dynamic systems, remains challenging. We therefore developed a novel approach that combines multi-level agent-based systems with spatial and temporal organization, allowing for a tuned representation of the transmission processes amongst the host population. We applied this method to model the spread of a PRRSv-like virus in pig farms, integrating the clinical consequences (conception and reproduction failures), in terms of animal husbandry practices. the results highlighted the importance to account for spatial and temporal structuring and herd management policies in epidemiological models.Indeed, disease-related abortions, inducing reassignments of sows in different batches, was shown to enhance the transmission process, favouring the persistence of the virus at the herd level. Supported by a domain-specific declarative language, our approach provides flexible and powerful solutions to address the issues of on-farm epidemics and broader public health concerns. The present application based on a simple SEIR model opens the way to the representation of more complex epidemiological systems, including more specific features such as maternally derived antibodies, vaccination, or dual infections, along with their respective clinical consequences on the management procedures.

## 1 INTRODUCTION

Understanding the mechanisms of pathogen spread is a key element for epidemic control in a highly structured population. This requires to capture the spatial and social structures,

defining the contact rates between individuals and groups of hosts in the population. Livestock management clearly illustrates that problematic, obeying predefined rules ensuring a balance between animal welfare, good sanitary conditions, and productivity. The spread of pathogens in a pig farm, managed with batch-rearing procedures, therefore represents an ideal application for the integration of an innovative organizational pattern within a multi-level agent-based modelling framework dedicated to epidemiological modelling.

To further understand the impact of batch management, housing, and possible deviations in herd management on the spread of pathogens at different scales, and to identify realistic levers, new modelling approaches had to be developed. To overcome the complexity of implementing such models in reliable, revisable and flexible simulation code, Artificial Intelligence (AI) methods were developed, leading to a new epidemiological modelling software, EMULSION (Picault et al., 2019).

In that view, in a previous study, we first developed a model of swine influenza A in pig farms, highlighting the impact of the spatio-temporal structure of the herd on the transmission dynamics and its impact on virus spread and control (Sicard et al., 2021a). However, in this study, influenza infections were not considered having any consequence in terms of animal management. Therefore, the next step was to account for the interplay between infectious dynamics and management practices. For this purpose, we developed an epidemiological model to represent the spread of a respiratory disease transmitted by direct contacts between animals (e.g. porcine reproductive and respiratory syndrome virus or porcine circovirus of type 2), and assuming clinical consequences leading to modifications of the management rules. These features can be frequently encountered in diseases such as the Porcine Reproductive and Respiratory Syndrome (PRRS).

To ensure realistic epidemiological modelling regarding field situation, including the contact structure between animals and different observation levels (farm, herd, individual, etc.), agent-based simulation (ABS) has proven its value (Roche et al., 2008). ABS provides methods for handling behaviours, interactions, and tracking of individuals. For further explicit representation of complex systems, multi-level agent-based simulation (MLABS) allows several scales (individuals, groups, batches, populations, etc.) to be associated with agents endowed with their own behaviours. Besides, MLABS makes it possible to separate procedural knowledge

(calculations and processes involved in stochastic epidemiological models, according to the modelling paradigm and scale: compartmental models, individual-based, metapopulations, etc.), and declarative knowledge (model structure, assumptions, description of groups and processes, parameter values, initial conditions), as set out in symbolic AI (Weyns, 2005; Mathieu et al., 2015, 2018). This separation of concerns provides the ability to make models modular and easy to use by defining independent processes (infection, population dynamics, trade movements, detection, etc.) which can be coupled, rather than a representation with a single, huge and tangled flow diagram.

We propose a prototype model architecture accounting for the complex interplay between pathogen transmission dynamics and consequences of clinical cases on herd management, by coupling a mechanistic multi-level agent-based modelling approach (EMULSION framework) with specific organizational considerations (Sicard et al., 2021b). We illustrate this approach through a PRRSv-like diseases spreading in a fine-grained realistic pig farm model.

# 2    MATERIALS AND METHODS

The EMULSION modelling framework enables the specification of different scenarios by varying the population dynamics in the breeding sectors (batch management, exceptions, etc.). These scenarios were used to assess the impact of clinical outcomes of infectious diseases on population and transmission dynamics at the herd level.

The management of the batches involved was the same as in Sicard et al. (2022) (sector allocation, stay duration, etc.). The model took into account insemination failure (with possible batch downgrading for infected sows), the different periods of gestation with their impact on the health status of piglets at birth (vertical transmission), and the management of sow renewal. Furthermore, the model was able to represent batch management at a fine-grained level (litter and pen), which provided the ability to represent zootechnical practices such as adoption or different grouping procedures.

## 2.1    EMULSION Framework

The model was developed using the EMULSION framework (Picault et al., 2019), which is dedicated to stochastic mechanistic epidemiological modelling. An essential concept of the framework

Figure 1: Structure of the organizational pattern (Sicard et al., 2021b). The agent *Organization* encapsulate an environment where agent *Group* is situated. Each agent *Group* encapsulates an environment where the atomic agents are situated. The pattern can be used recursively, i.e. an agent *Group* can itself be an organization. The environment in the pattern can be either spatial or social.

is the separation between knowledge representation (the model as a structured text), and the simulation processes (provided by a generic engine which reads and execute the model description).

The EMULSION framework, extended with its organizational extension (Sicard et al., 2021b), was used to account for the complex herd structure in both space and time, including multi-level aspects. An organization is an entity made up of groups to which individuals belong. Organizations and groups encapsulate environments that correspond to spaces where agents are located (either groups or individuals). The organizational pattern systematically describes three levels: organization, group, and individual.

A particular feature of the pattern is its ability to be used recursively. In other words, a group can itself be an organization (thus becoming a sub-organisation) (Figure 1), thereby describing multi-level dynamics and relationships between levels.

## 2.2 Population dynamics

The pig production herd was raised according to a seven-batch-rearing system, the main management practice held in France, which was fully described in Sicard et al. (2022). Two subpopulations, breeding sows and growing pigs, were represented, structured and managed according to husbandry constraints d'Agriculture de Bretagne (2010) . The farm was managed through a

Figure 2: Illustration of the duration of different physiological stages in relation to housing, with a dotted arrow indicating piglet production from sows.

7-batch-rearing system with a 21-day between-batch interval, and all-in-all-out procedures. The batches remained consistent, i.e. within a same batch all animals were in the same physiological state at the same time, depending on whether they were sows or piglets, obeying an all-in-all-out procedure.

Sows evolved through three physiological states over 147 days : insemination (24 days), gestating (85 days) and farrowing/lactating (28 days). Growing pigs evolved through three stages over 182 days before being sent to the slaughterhouse: farrowing/suckling (28 days), post-weaning (40 days) and finishing (114 days) (Table 2, Fig. 3 and 4). Each physiological stage corresponded to a specific physical sector of the farm.

The *housing* organization ensures that the spatial sectorial structure of the housing is ade-

Figure 3: Representation of the *state machine* `physiological_step` managing the transitions of the physiological stages. The transitions between states occurred after a stay duration in the state. Sows followed a cycle consisting of *Insemination*, *Gestating* and *Lactating*, and piglets evolved through the *Suckling*, *Post-weaning* and *Finishing* states before leaving the system for the slaughterhouse.

```
physiologicalStep:
    desc: 'physiological step evolution'
    states:
      - Insemination:
          name: 'Insemination'
          desc: 'Insemination period (only for sows)'
          duration: insemination_duration
          on_enter:
            - become: gestatingSow
              proba: is_Sow
      - Gestating:
          name: 'Gestating'
          desc: 'Gestating period (only for sows)'
          duration: gestating_duration
          on_enter:
            - become: inseminateSow
              proba: 1
      - Farrowing:
          name: 'Farrowing'
          desc: 'Farrowing period (for sows and
              piglets)'
          duration: farrowing_duration
          on_enter:
            - become: to_cull_proto
              proba: proba_to_cull
      - PostWeaning:
          name: 'PostWeaning'
          desc: 'Post-weaning period (only for
              piglets)'
          duration: post_weaning_duration
      - Finishing:
          name: 'finishing'
          desc: 'Finishing period (only for piglets)'
          duration: finishing_duration
      - Exit:
          name: 'Exit'
          desc: 'Exit the system (slaughterhouse,
              culled, etc.)'
          autoremove: True

    transitions:
      - from: Insemination
        to: Gestating
        proba: 1
      - from: Gestating
        to: Farrowing
        proba: 1
      - from: Farrowing
        to: Insemination
        proba: is_Sow
        on_cross:
            - clone: new_Sow
              proba: proba_produce
      - from: Farrowing
        to: PostWeaning
        proba: is_Piglet
      - from: PostWeaning
        to: Finishing
        proba: 1
      - from: Finishing
        to: Exit
        proba: 1
```

Figure 4: The `physiologicalStep` state machine in the EMULSION framework is used to model the physiological states of sows during the breeding cycle. When a sow enters the *Insemination* state, it transitions to the *Gestating* state and undergoes a check for insemination success or failure. If the sow enters the *Farrowing* state, a probability of culling is applied, and renewal gilts are introduced for the next breeding cycle. The renewal of sows occurs during the transition between the *Farrowing* and *Insemination* states (using the `on_cross` event).

quate for the physiological needs of the individuals. The sectorial organizations are divided into downstream levels corresponding to the rooms in the herd. Each level can be considered as an organization, which can further divided into downstream sublevels. The rooms are subdivided into pens to represent the direct and indirect contacts of animals within and between pens.

Batches were managed by several organizations: *Batches* for main herd management, *Litter* for making the link between breeding sows and their piglets, *Litter_group* for gathering purpose in nursery pens, and *Housing* specifying the exact location of each animal (or group of animals) in corresponding sectors, rooms, and pens.

At initialization, 29 sows were homogeneously distributed among the 7-batch organization. At farrowing, newborn piglets were assigned to the same batch and same pen as their mother. The *litter* organization was designed as the dams and their relative piglets, located in the same space (pens) in farrowing rooms. This organizational level consisted of 18 pens, which could be used to accommodate all sows in the event of overcrowding caused by insemination failures or abortions that occur during gestation in other batches. Sows were alternatively located in designated organizational spaces, while piglets were housed in the same pen as their respective mothers during farrowing.

*litter_group* was designed to represent pig gathering policy in nursery rooms after weaning. Indeed, pig litters are frequently gathered into larger groups within pens when entering the nursery sector. In our model, it was assumed that each pen in the nursery rooms housed two litters from the farrowing rooms. The location of the litters within the pens was managed by one of the *housing* sub-organisations.

Herd renewal might be a factor influencing disease spread by introducing susceptible animals into the system. In commercial pig production, sows are selected for replacement based on productivity criteria. For example, old sows are known to have smaller litters, and farmers cannot afford to keep sows that experience multiple gestation failures. In the present model, for the sake of illustration, the decision to cull based on their condition (*condition_to_cull*) was made :

- sows with parity higher than 5,

- sows with more than 5 gestation failures.

```
litter:
  name: 'litter'
  desc: "litter organization (social aspect)"
  execute_process:
    - allocate
  spaces:
    name: 'litters'
    description: 'litters'
    allocation:
      - if: 'is_Piglet'
        then: 'with_source()'
      - if: 'is_Sow'
        then: alternate_free(spaces=ALL, filter=[Sow, batches])
    nodes:
      litter01:
        informations:
          total_I:
            value: 0
      ...
```

Figure 5: Statement of the organisation `litter`. The organization comprised 18 nodes, with sows being assigned to each node alternately using the `alternate_free` method. Within each node, piglets, and dams were housed together in the same pen using the `with_source()` method, ensuring that they shared similar social and spatial environments.

The maximum number of sows that could be replaced at each batch-cycle was set to 2 and adjusted to ensure a stable population in each batch, ranging between the initial number of sows in the herd (16 sows per batch) and the total number of pens in farrowing room (18 pens). The renewal was managed by the *culling* state machine accounting for three states : *to_keep* corresponding to sows that will be not renewed, *to_cull* corresponding to sows that will be renewed, and *culled* corresponding to sows that leave the system. The decision on the status of the sows is made when entering in farrowing room; after the lactation period, renewal gilts are introduced for the next reproduction cycle.

Insemination failure was represented by the state machine *inseminationStatus*. On entering the insemination sector (corresponding to the gestating state of the physiologicalStep state machine), sows were inseminated (inseminate status). X days after insemination, sows are checked for gestation, with a failure probability defined as *proba_failure_ins*. Sows that were successfully inseminated were moved to *SuccessInf* state. Sows that had failed insemination were retrograded from two previous batches. Owing to the 7 batch-farrowing system, an insemination failure for

| Parameter | Description | Value | Source |
|---|---|---|---|
| $\beta$ | direct transmission rate | 0.24 | Rose et al. (2015) |
| $\beta_{ind}$ | indirect transmission rate | $\beta/10$ | Andraud et al. (2008) |
| $\gamma$ | recovery rate | 0.18 | Nodelijk et al. (2000) |
| duration in M | gamma law | $\Gamma(\text{shape} = 3.6,$ $\text{scale} = 1.35\ \text{days})$ | Andraud et al. (2019) |

Table 1: Table of epidemiological parameter values

154  a sow in batch $N$ led to a transfer into batch $N - 2$, for new insemination attempt. Such event
155  will be next mentioned as a batch reassignment event.

## 2.3  Health states

Four health states were considered: animals protected by maternal immunity (M), susceptible
(S), infectious (I), and recovered (R). These health states were managed by the state machine
*health_state* (Figure 3 The state $M$, corresponding to a piglet protected by maternal immunity,
was managed separately by the state machine *maternal_immunity*. The epidemiological param-
eters were based on a PRRSv-like disease, and are reported in the table 1. The parameter $\beta_{ind}$
represents the rate of transmission resulting from occasional contacts between individuals from
adjacent pens.

To account for the complex spatial structure of the animal housing, calculating the force of
infection, including the direct pairwise contact in the pens, was a cumbersome task. To facilitate
the representation of transmission routes and increase the flexibility of the contact structure,
a graphic-based approach was adopted. Specifically, the housing system was represented as
a graph, where the nodes corresponded to the physical environmental spaces such as pens,
corridors, and rooms, and the links represented the interactions between these spaces. The
links were weighted by the epidemiological information of each space. This approach provided
a comprehensive and flexible representation of the transmission dynamics within the housing
system.

Specifically, each space in the housing system was associated with the number of infectious
animals it contained, and this information was propagated through the graph. The cumulative
information obtained from the graph was then used to compute the force of infection:

$$\text{force\_of\_infection} = \beta \times \text{info\_total\_I\_my\_pen} \tag{1}$$

| Scenario | Description |
|---|---|
| Scenario 1 | Sows grouped by 6 without batch reassignment |
| Scenario 2 | Sows grouped by 6 with batch reassignment |
| Scenario 3 | All-in-One grouped sows without batch reassignment |
| Scenario 4 | All-in-One grouped sows with batch reassignment |

Table 2: Description of the four scenarios. Each scenario corresponds to a combination of grouping type in the gestation sector (grouped by 6 or All-in-One), and batch management policies (batch reassignment due to insemination failure or batch stability)

where *info_total_I_my_pen* corresponded to the specific function of the EMULSION framework to get the value of the total number of infectious individuals (*total_I*) information of the current space (*my_pen*).

Piglets' epidemiological status at birth was assumed dependent on the period of gestation the sows were infected. Sow infected in the first third of their gestation produce susceptible piglets; Sow infected in the second third of their gestation produce piglets infected through transplacental transmission; finally, piglets born to sows infected in the last phase of the gestation period acquire maternally derived antibodies in the "M" state.

## 2.4 Scenarios

Four scenarios were established to represent several types of management, taking into account the exchange of sows between batches in case of insemination failure, the type of grouping in gestating, and the rate of occasional contact (table 2.4). Each scenario was run with 100 stochastic replicates over a period of 1500 days, including a burning period of two reproductive cycles ($2 \times 147$days). The virus was introduced by an infected sow in batch 1, at the beginning of the third reproductive cycle of the batch, assuming the introduction of an infected gilt into the system (294 days).

## 3 RESULTS

The results provided a measure of the impact of management changes (grouping) of breeding sows on the infectious dynamics. Scenarios with no grouping in the gestation sector, and one room per batch, showed a weak impact of batch changes due to insemination failure. For the scenarios with $\beta_{ind}$ of 0 and $\beta/10$, the dynamic profiles were similar (Figure 6).

In the scenarios with $\beta_{ind}$ of 0, the first peak occurred approximately 34 days after virus was

introduced and corresponded to the entry into the gestation sector. As sows in the same batch were mixed, the virus spread rapidly within the batch. The second peak, about 85 days after the first, corresponds to farrowing sector. The following peak, about 28 days later, corresponded to piglets entering the post-weaning sector. In the farrowing sector, each pen contained one litter consisting of sow and her piglets, and the pens were assumed independent, with no possible contact with neighbouring pens. With a $\beta_{ind}$ value of 0, only within-pen transmission occurred. Conversely, in the post-weaning sector, where pens were not independent, litters were grouped in pairs in pens, and transmission occurred between adjacent pens with $\beta_{ind} = \beta/10$. It was shown that batch changes for infected sows following failed insemination in the $n-2$ batch in the insemination sector broke the infectious dynamic within the batch.

The duration of infection was 56 days, which is longer than the period between entry into the insemination sector and the detection of insemination failure (42 days). Therefore, a retrograded infected sow could potentially infect other individuals, at least in the insemination sector, and potentially as far as the gestating sector (if a sow was infected a few days before being retrograded, it would arrive in the gestating sector of its new batch at 36 days, and could be infectious for about 20 days). For the scenarios without grouping, changes to nominal batch-rearing management did not have a notable impact on the transmission dynamics. For the scenarios with grouping (per 6) in the gestating sector, exceptions to batch rearing substantially impacted the infection dynamics, with transmissions occurring between non-adjacent pens in fully susceptible groups of sows.

For the scenarios with a value of $\beta_{ind}$ of 0 (Figure 6), the first peak corresponded to the entry into the gestating sector. Due to the grouping by 6 of the sows in this sector, the batch reassignment strongly impacted the transmission dynamics, with higher peaks of incidence due to the potential introduction of infected sows in fully susceptible pens.

Figure 6: Infection dynamics for scenarios with grouping in gestating sector. This shows the median number of infected sows over time across the whole farm after the introduction of an infected sow in batch 1 at 294 days.

# 4   DISCUSSION

We developed a model to better understand the interplay between social and spatial organization of a pig production herd and infection dynamics. Indeed, several pathogens (e.g. PRRSv, PCV-2, influenza viruses, *Mycoplasma hypopneumoniae*...) can yield to deviations in herd management due to clinical expressions in pigs, impairing the nominal management to be operated. The complex interactions between disease management strategies and their impact on herd organization, together with the dynamics of disease spread, have not yet been fully accounted for in the current model due to the complexity it introduces in the model design. To achieve this, we applied an artificial intelligence-based approach. We introduced an original multi-level agent-based design pattern to capture organizational features involved in the complexity of highly structured populations in time and space. This approach was associated with a dedicated modelling language to facilitate the specification of such organizations without writing computer code, and it was integrated into the EMULSION framework. Our approach facilitated the representation of the complex spatio-temporal herd structure, enabling us to conduct a comprehensive study of the system.

Several models were developed to represent the spread of different pathogens in pig production units Andraud and Rose (2020). Swine influenza virus, PCV-2, or hepatitis E virus were indeed fields of application for models with different paradigms, from individual based approaches to population based models, depending on the transmission characteristics of the pathogens. Multi-level Agent-based Systems provide solutions for unifying these modelling paradigms using a common framework, with high Readability, Reproducibility, and Flexibility (RRF). The adds-on of our organizational design-pattern offers the opportunity to tackle population structures with fine-grained representations of their epidemiological consequences, keeping the above-mentioned (RRF) advantages. This was recently illustrated with a model representing the transmission of a swine influenza A virus in a pig herds with different spatial configurations Sicard et al. (2022). Previous models represented the impact of management practices on the transmission dynamics, to assess how husbandry practices could be modified to better handle health issues at the herd level Cador et al. (2016); Suksamran et al. (2017) Clinical aspects and their potential consequences, in terms of management and infection dynamics, were nevertheless rarely considered. PRRS virus is recognized as a major economic burden for swine producers, inducing huge

loss due to growth retardation, abortions or reproduction failures, birth of stillborn fetuses or weak-condition piglets Le Coz (2007); Renken et al. (2021); Charpin et al. (2012). Such clinical outcomes necessarily induce exception in the management of the herds, affecting, in turn, the transmission dynamics. We therefore developed a model, accounting for organizational features, to study the impact of such disease-related exceptions on the transmission of an infectious agent within a pig herd.

The model primarily focuses on representing the dynamics in the breeding sectors and their impact on the whole farm. Our Results highlight the roles played by various transmission routes, including batch change of sows after insemination failure, sow grouping in the gestating sector, and indirect contact rate ($\beta_{ind}$). Introduction of infectious sows in susceptible batches clearly increased the risk of persistence of the virus on farm.

Mixing animals from different batches can partially explain the observed infectious dynamics in the field. However, to effectively control the spread of infection, it is necessary to further investigate the underlying transmission mechanisms and develop farm-specific solutions. Our model identified the primary transmission routes and the impact of reinfection on the breeding population. These factors could lead to infection in maternity piglets and, ultimately, active immunity that could lead to virus extinction. While establishing effective immunity in piglets with maternal immunity can be challenging, our previous research highlighted its potential as a control measure for Influenza A (Sicard et al., 2022). This study considered only deviations of management due to insemination failures, which could correspond to clinical consequences for sows infected by PRRSv during early gestation, having low conception rate. However, the consequences of PRRSv infections are dramatic for animals of all physiological stages. Late abortions would lead to mixing animals from different batches. Culling rate might also be increased, inducing the introduction of renewal gilts, feeling the pool of susceptible animals. In growing pigs, birth of piglet of weak condition, or growth retardation due to infections could favour mingling of animals from different litters in nursery pens. These impacts may have indirect consequences on herd management, leading to exceptions in nominal management, such as mixing animals at different physiological stages. Our study showed that exceptions due to batch reassignment for sows played an important role in infectious dynamics. Our proposed methodological solution, which used artificial intelligence and organizational design patterns

for multi-level agent-based simulation, provides a concrete way to represent these phenomena. However, the model will need to be extended to account for the virus's impact on the whole farm's management of exceptions.

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# References

Andraud, M., Grasland, B., Durand, B., Cariolet, R., Jestin, A., Madec, F., and Rose, N. (2008). Quantification of porcine circovirus type 2 (PCV-2) within- and between-pen transmission in pigs. *Veterinary Research*, 39(5):43.

Andraud, M., Halasa, T., Boklund, A., and Rose, N. (2019). Threat to the French Swine Industry of African Swine Fever: Surveillance, Spread, and Control Perspectives. *Frontiers in Veterinary Science*, 6:248.

Andraud, M. and Rose, N. (2020). Modelling infectious viral diseases in swine populations: a state of the art. *Porcine Health Management*, 6(1):22.

Cador, C., Hervé, S., Andraud, M., Gorin, S., Paboeuf, F., Barbier, N., Quéguiner, S., Deblanc, C., Simon, G., and Rose, N. (2016). Maternally-derived antibodies do not prevent transmission of swine influenza A virus between pigs. *Vet.Res.*, 47(1).

Charpin, C., Mahe, S., Keranflec'H, A., Madec, F., Belloc, C., Cariolet, R., Potier, F. L., and Rose, N. (2012). Estimation du potentiel infectieux en fonction du temps de porcs infectés par le virus du Syndrome Dysgénésique et Respiratoire Porcin (SDRP) :. page 6.

d'Agriculture de Bretagne, C. (2010). Les conduites en bande - Cohérence de la cha\^ine de bâtiments, Organisation du travail, Truies en groupe.

Le Coz, P. (2007). SDRP - L'impact économique de la maladie : quel est le coût actuel en élevage?

Mathieu, P., Morvan, G., and Picault, S. (2018). Multi-level agent-based simulations: Four design patterns. *Simulation Modelling Practice and Theory*, 83:51–64.

Mathieu, P., Picault, S., and Secq, Y. (2015). Design patterns for environments in multi-agent simulations. In Chen, Q., Torroni, P., Villata, S., Hsu, J., and Omicini, A., editors, *Proceedings of the 18th Conference on Principles and Practice of Multi-Agent Systems (PRIMA 2015)*, volume 9387, pages 678–686. Springer.

Nodelijk, G., De Jong, M. C. M., Van Nes, A., Vernooy, J. C. M., Van Leengoed, L. A. M. G., Pol, J. M. A., and Verheijden, J. H. M. (2000). Introduction, persistence and fade-out of porcine reproductive and respiratory syndrome virus in a Dutch breeding herd: a mathematical analysis. *Epidemiology and Infection*, 124(1):173–182.

Picault, S., Huang, Y.-L., Sicard, V., Arnoux, S., Beaunée, G., and Ezanno, P. (2019). EMULSION: Transparent and flexible multiscale stochastic models in human, animal and plant epidemiology. *PLOS Computational Biology*, 15(9):e1007342.

Renken, C., Nathues, C., Swam, H., Fiebig, K., Weiss, C., Eddicks, M., Ritzmann, M., and Nathues, H. (2021). Application of an economic calculator to determine the cost of porcine reproductive and respiratory syndrome at farm-level in 21 pig herds in Germany. *Porcine Health Management*, 7(1):3.

Roche, B., Guégan, J.-F., and Bousquet, F. (2008). Multi-agent systems in epidemiology: a first step for computational biology in the study of vector-borne disease transmission. *BMC Bioinformatics*, 9.

Rose, N., Renson, P., Andraud, M., Paboeuf, F., Le Potier, M., and Bourry, O. (2015). Porcine reproductive and respiratory syndrome virus (PRRSv) modified-live vaccine reduces virus transmission in experimental conditions. *Vaccine*, 33(21):2493–2499.

Sicard, V., Andraud, M., and Picault, S. (2021a). L'organisation comme Design Pattern dans les systèmes multi-agents multi-niveaux. In *Actes des Journées Francophones sur les Systèmes Multi-Agents (JFSMA) 21*, pages 73–82. Cépaduès.

Sicard, V., Andraud, M., and Picault, S. (2021b). Organization as a Multi-level Design Pattern for Agent-based Simulation of Complex Systems. In *Proceedings of the 13th International Conference on Agents and Artificial Intelligence*, pages 232–241, Austria. SCITEPRESS - Science and Technology Publications.

Sicard, V., Picault, S., and Andraud, M. (2022). Coupling spatial and temporal structure in batch rearing modelling for understanding the spread of the swine influenza a. In *Society for Veterinary Epidemiology and Preventive Medicine*, page 11. SVEPM.

Suksamran, J., Lenbury, Y., Satiracoo, P., and Rattanakul, C. (2017). A model for porcine reproductive and respiratory syndrome with time-dependent infection rate: traveling wave solution. *Advances in Difference Equations*, 2017(1):215.

Weyns, D., editor (2005). *Environments for multi-agent systems: first international workshop, E4MAS 2004, New York, NY, July 19, 2004 ; revised selected papers*. Number 3374 in Lecture notes in computer science Lecture notes in artificial intelligence. Springer, Berlin. OCLC: 253920904.