Deep mechanistic model: Integrating deep learning and stochastic mechanistic approaches for Bovine Respiratory Diseases diagnosis and epidemiological forecasting

Theophile Ghislain Loic Eyango Tabi, Maud Rouault, Victoria Potdevin, Xavier l'Hostis, Sébastien Picault, Nicolas Parisey

DEEP MECHANISTIC MODEL: INTEGRATING DEEP LEARNING AND STOCHASTIC MECHANISTIC APPROACHES FOR BOVINE RESPIRATORY DISEASES DIAGNOSIS AND EPIDEMIOLOGICAL FORECASTING

T.G.L. EYANGO TABI*, M. ROUAULT, V. POTDEVIN, X. L'HOSTIS, S. ASSIE, S. PICAULT AND N. PARISEY

SUMMARY

Bovine Respiratory Disease (BRD) poses a significant challenge in beef fattening due to its complex causes. Relying solely on data-driven sensor methods for early detection may yield false alarms. This paper introduces an innovative approach that integrates a deep learning model with a BRD mechanistic model, utilizing pulmonary ultrasounds and clinical exams as sensor data and ground truth, respectively. By employing reliable clinical diagnostics, three crucial biological parameters were inferred, enabling the forecast of the number of asymptomatic animals up to 30 days. The deep learning model achieves 70% accuracy in diagnosis, and the BRD mechanistic model forecasts disease dynamics with less than 5% error. However, the hybrid method's weakness lies in clinical exams' uncertainty for some animal diagnosis, and improvements to the BRD model have been addressed in existing literature. Future work could explore incorporating biological exams or utilizing a pathogen-specific model for enhanced accuracy.

INTRODUCTION

The Bovine Respiratory Disease (BRD) poses significant challenges to farmers, as it results in substantial economic losses, accounting for as much as 20% of farmers' incomes (Bareille et al., 2009). This disease raises critical concerns for animal welfare, as it can lead to fatal pneumonia in calves (Delabouglise et al., 2017; Engler et al., 2014). The predominant treatment for BRD relies on antimicrobials, however, practices like systematic collective treatments and misdiagnosed BRD, including false detection, contribute to antimicrobial misuse. It is crucial to ensure proper and judicious administration of these antimicrobials to prevent the emergence of antibiotic resistance. The complexity of diagnosing BRD stems from numerous factors, including the involvement of multiple pathogens such as bacteria and viruses, as well as susceptibility to external and environmental influences like weaning, stress, breed, immunity, and farming conditions (Hay et al., 2016; Kudirkiene et al., 2021). On a more positive note, farms are generating a wealth of valuable data, providing significant potential for insights. Farms are also increasingly incorporating sensor technologies to enhance and automate data collection. Consequently, precision livestock farming emerges as a promising tool for real-time

* Theophile Ghislain Loïc Eyango Tabi, Bioepar, INRAE, Oniris, 44300, Nantes, France
Email: loic.eyango@adventiel.fr

monitoring and farm management, with the potential to improve animal health and welfare (Berckmans, 2014).

Various approaches have been explored to leverage farm data and study the spread of diseases. One type uses data-driven methods in sensors, excelling at detecting straightforward symptoms or events, such as heat (Kosanovic et al., 2022), heat stress (Hoffman et al., 2022), calving and hyperthermia. However, these sensors have limitations when it comes to complex diseases like BRD, which involve intricate underlying epidemiological processes (Concordet et al., 2022; Pfeiffer et al., 2022). For instance, hyperthermia, a symptom of BRD, can result from causes other than BRD, such as overexertion. Thus, relying solely on early detection of hyperthermia infectious episodes may also lead to false alarms. Additionally, cattle tend to hide early symptoms as a survival behaviour (Griffin, 2010), reducing the quantity of observations needed to adjust data-driven methods. Alternatively, knowledge-driven methods, like mechanistic models, are widely used to understand how pathogens spread across different scales and according to contrasted scenarios, from individual animals to entire regions (Ezanno et al., 2020). As such, mechanistic models have contributed a lot to modelling and understanding the spread of pathogens involved in BRD (Picault et al., 2022; Sorin-Dupont et al., 2023), however their calibration remains a substantial challenge.

The hypothesis of this paper suggests that by combining data-driven and knowledge-driven methods, an integrated and innovative approach can be developed. This approach is applied to automatically diagnose male beef cattle and forecast the dynamics of BRD. The designed workflow integrates a spatiotemporal convolutional neural network with a stochastic mechanistic models and pulmonary ultrasound videos used as sensor data.

MATERIALS AND METHODS

Figure 1 illustrates the overall workflow and unfolds as follows: in the first section (Fig.1a), pulmonary ultrasound videos are employed as sensor data. These videos were selected to test the pipeline because they provide an internal view of the lungs, potentially serving as a reliable sensor for detecting respiratory symptoms. Moving to the second section (Fig.1b), clinical observations (categorized as either healthy or diseased) are considered as ground truth. These states are determined by a veterinarian through clinical assessments, including physiological parameters like rectal temperatures and other clinical signs (cough, nasal or ocular discharge, depression, etc.). The underlying hypothesis is that animals exhibiting a certain number of clinical signs (symptomatic) are considered diseased. In the third section (Fig.1c), sensor data and ground truth are utilized to train and compare multiple deep learning models, specifically spatiotemporal convolutional neural networks. Their objective is to accurately predict the clinical health state of each animal. During training, the predictions are statistically evaluated for potential use in real farm conditions. However, in operational conditions, clinical assessments will not be necessary as the best-trained deep learning model would automatically predict clinical health states using pulmonary ultrasound videos. In the last section (Fig.1d), reliable clinical health states serve as input to calibrate parameters of a mechanistic model. The performance of various parameter inference methods was compared for three crucial parameters of an average pathogen stochastic mechanistic model (Picault et al., 2022). This calibration enables a 30-day forecast of the number of asymptomatic animals within specific batches across two farms with contrasting configurations.

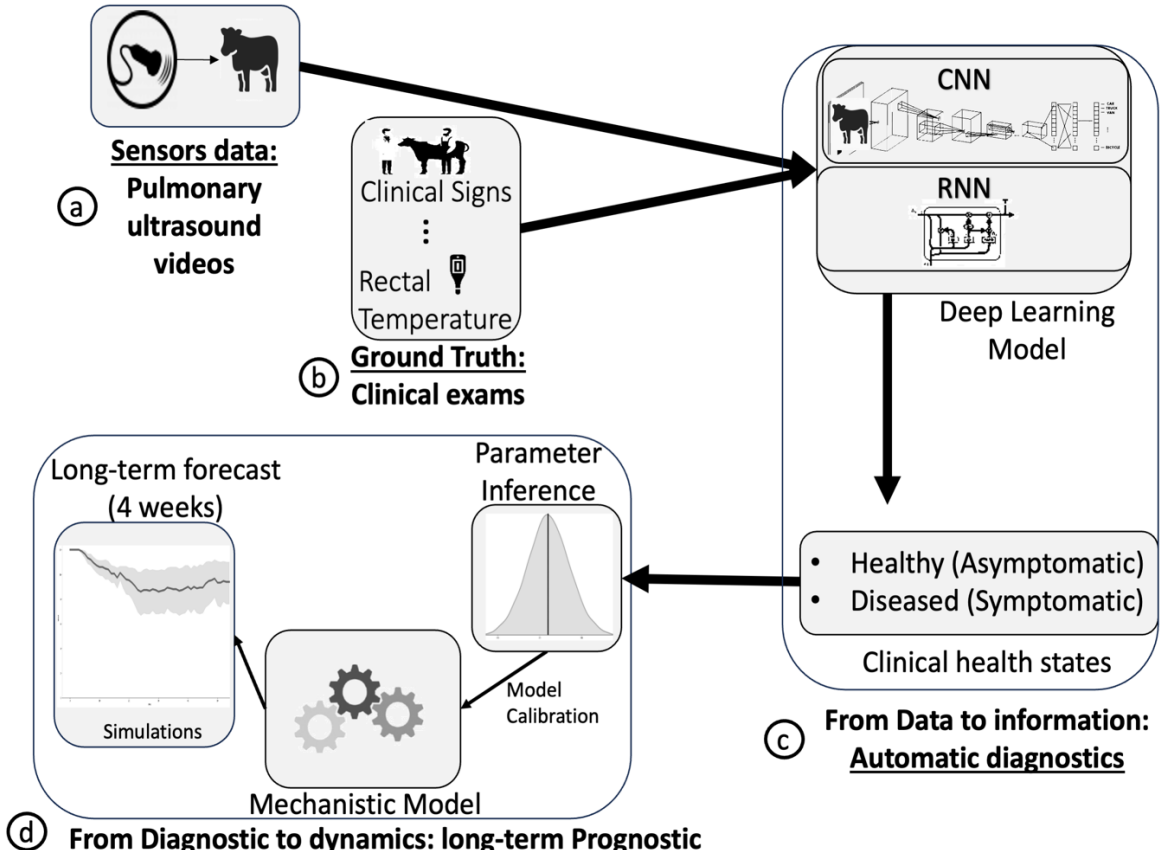

Figure 1. Workflow of the "deep mechanistic model" approach. This hybrid approach integrates a deep learning model (data-driven) with a mechanistic model (knowledge-driven)

Data acquisition, sensor data and ground truth

The experiment encompassed nine fattening farms, each simultaneously managing up to three batches of male beef cattle, with each batch comprising eight to twelve calves. In terms of breed distribution, 78% of the cattle were Charolais, 12% Limousin, and the remaining 10% were of mixed races. The Charolais breed was predominantly chosen due to their clearer display of clinical symptoms. Data collection started on the day the cattle arrived at the farm (Day 0) and extended for one month, considering it as the period when cattle are most susceptible to BRD (Babcock et al., 2009). Data collection spanned from January 2023 to June 2023, encompassing a total of 480 beef cattle in the experimentation.

Sensor data (Fig.1a): portable ultrasound scanners were used to assess the animals' lungs on multiple days: Day 0, Day 2, Day 5, Day 14, Day 21, and Day 28. The selection of dates varied across farms, based on the availability of farmers and a veterinarian. The ultrasound scanner captured lung images in video format, with 28 frames per second in black and white, lasting up to 20 seconds each, and 480x560px resolution. The animals' lungs were divided into eight intercostal zones, following a standardized scanning protocol from the shoulder to the stomach. A veterinarian validated the dataset to ensure accuracy. Recording a video with an ultrasound scanner is time-consuming, tedious, and challenging, requiring animals to be kept in a fixed position, which is not an easy task. This led to prioritizing cases for study, considering only lesions larger than 1 cm^2 as meaningful (Masset et al., 2022). For each intercostal zone, a video of only the largest lesions is saved. On Day 0, one-third of each batch was examined, while from Day 2 to Day 28, all animals in a selected batch were examined. To maintain balance in

the dataset, videos of clinically healthy lungs (without lesions) were also recorded, resulting in a total of 255 lung ultrasound videos.

Ground truth (Fig.1b): several veterinarians participated in annotating the ground truth data, having undergone the same training to minimize annotation bias. The determination of ground truth for identifying diseased animals relied on clinical assessments. The decision rule utilized was established in various publications (Timsit et al., 2019, 2011). An animal was considered diseased if it had a rectal temperature exceeding 39.7°C and displayed at least one clinical symptom. These clinical symptoms were defined based on a clinical assessment table (Table 1) established by veterinarians. This method of diagnosing diseased animals is widespread in France, with three out of nine farms in this experiment already using it. Every animal in each batch underwent clinical examinations, following the same frequency as the collection of sensor data.

Table 1. Data dictionary of the clinical assessments

Observable Symptoms	**Tiredness**	**Shape of flank**	**Nasal discharge**	**Cough**	**Ocular discharge**	**Breathing amplitude**	**Breathing rate**
Levels	Absent, Mild, Severe	Hollow, Flat, Rounded	Absent, Mucous, Purulent, Serous	Absent, Weak, Strong	Absent, Mucous, Purulent, Serous	Normal, Augmented	Regular, Irregular

From Data to information: automatic diagnostics (Fig.1c)

Data Preprocessing: four steps were taken in data preparation process. Initially, the distribution of the entire dataset of pulmonary ultrasound videos was adjusted to address a significant class imbalance. Only 23.2% of videos belonged to diseased animals, while 76.8% belonged to healthy animals. To rectify this, a downsampling strategy was employed, using stratified random sampling considering factors like the intercostal zone, lesion size, lesion count, and the day of clinical assessment. In the second step, the dataset was split with a random shuffle: 60% for training (80 videos), 19% for validation (22 videos), and 13% for testing the model's performance (16 videos). The validation dataset served to adjust the model's weights during training, while the test set was exclusively used for accuracy evaluation after training. In the final step, ultrasound videos were cropped to eliminate areas containing text or watermarks.

Handling ultrasound videos is challenging due to varying frame counts and noisy images. Some videos were shorter than expected due to technical issues related to the ultrasound scanner. A straightforward solution involved extracting images from the videos until reaching a maximum count. If a video had fewer images, the missing frames would be filled with zeros, which is a method similar to handling text sequences.

Deep learning model: a video contains both spatial information within individual frames and temporal information across the entire sequence. To effectively address both aspects in video analysis, a hybrid architecture, specifically a spatiotemporal convolutional neural network was chosen. In our approach, we combined convolutional layers (CNN) with recurrent layers (RNN). The convolutional layers focus on extracting spatial features, such as lesions, pleura lines, or any other relevant anatomical details. Meanwhile the recurrent layers capture

temporal information, which pertains to the sequence or frequency of appearance of spatial features.

For the training phase (Fig.2), various convolutional layer architectures (spatial feature extractor) were compared. Depending on the number of layers, the depth, the structure, different architectures will extract different spatial features. The tested architectures include five classical networks pre-trained on imagenet, such as efficientNetB7, inceptionResnetV2, inceptionV3, VGG16, and a late fusion ensemble model of inceptionV3 with inceptionResnetV2. The temporal layer architecture is composed of eight layers: the first with sixteen neurons, the second with eight neurons, followed by a dropout layer that suppressed 40% of the neurons, and a final dense layer with eight neurons using a ReLU activation function. The classification layer employes a softmax function with two output neurons. The loss function used is a sparse categorical cross-entropy with an Adam optimizer. In conclusion, this model analyses an entire pulmonary video and predicts the clinical health state (diseased or healthy).

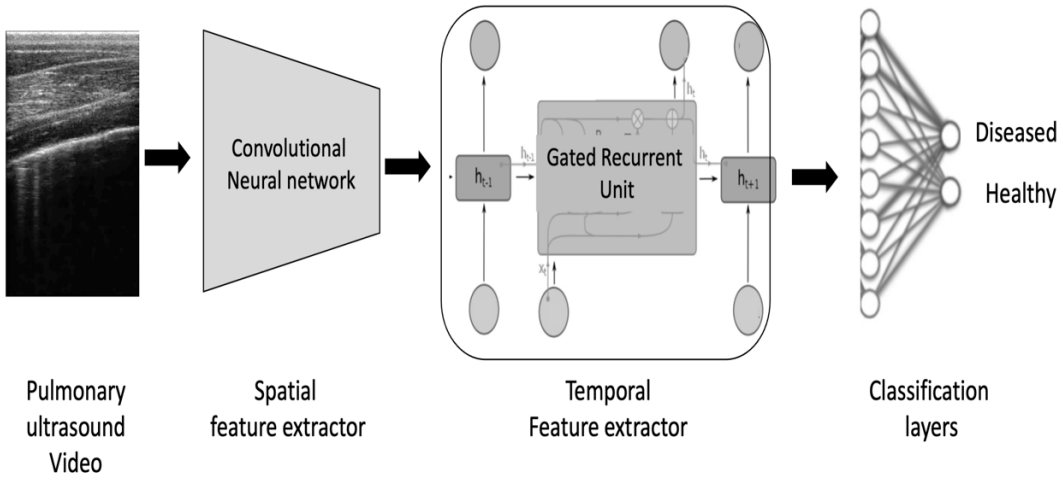

Figure 2. Deep learning Architecture Trained

Evaluation: to evaluate the model's performance, four essential metrics were considered. The *weighted precision* measures the proportion of correctly identified positive cases among all cases predicted as positive. The *weighted recall* reflects the ability of the model to identify many actual positive cases, providing insights into the model's capacity to capture relevant instances. The *weighted F1-score*, as the harmonic mean of precision and recall, offers a balanced assessment, considering both false positives and false negatives. Lastly, the *accuracy* indicates the overall proportion of videos that were correctly classified, serving as a general measure of the model's predictive power and overall performance. These metrics together provide a comprehensive understanding of the model's effectiveness in distinguishing between healthy and diseased cases in the pulmonary ultrasound videos.

From diagnostics to disease dynamic: prognostic (Fig.1d)

Mechanistic model: to date, only two mechanistic models for BRD have been published. The model introduced in (Picault et al., 2019a) was mechanistic (to explicitly represent processes), stochastic (to account for intrinsic variability in biological processes), and individual-based (to ensure a fine-grained detail level). This model aimed to investigate the

spread of BRD in French fattening pens by capturing the evolution of infection, emergence of clinical signs, detection, and subsequent treatment. To tackle the limited knowledge about interactions between multiple BRD pathogens, model parameters were calibrated assuming an average pathogen infection (Picault et al., 2022). A sensitivity analysis was also carried out to understand its behaviour and the impact of parameter uncertainty. Results emphasized the significance of parameters such as the pathogen transmission rate, the average duration in the infectious state, and the average duration in the pre-infectious state, crucial for controlling antimicrobial usage and mortality rates.

This study employed this average pathogen BRD model (Fig.3), utilizing the three biological parameters as essential input, with the output focusing on the count of symptomatic animals, encompassing those exhibiting both mild and severe clinical signs. Model predictions were given with a 12-hour time grain, aligning with the interval between successive visual assessments of beef cattle during feeding. Implementation was facilitated by the EMULSION platform (Picault et al., 2019b), allowing the depiction of all model components in a human-readable, flexible structured text file processed by a generic simulation engine. This facilitates collaboration and model refinement by scientists with diverse backgrounds, including veterinarians and epidemiologists.

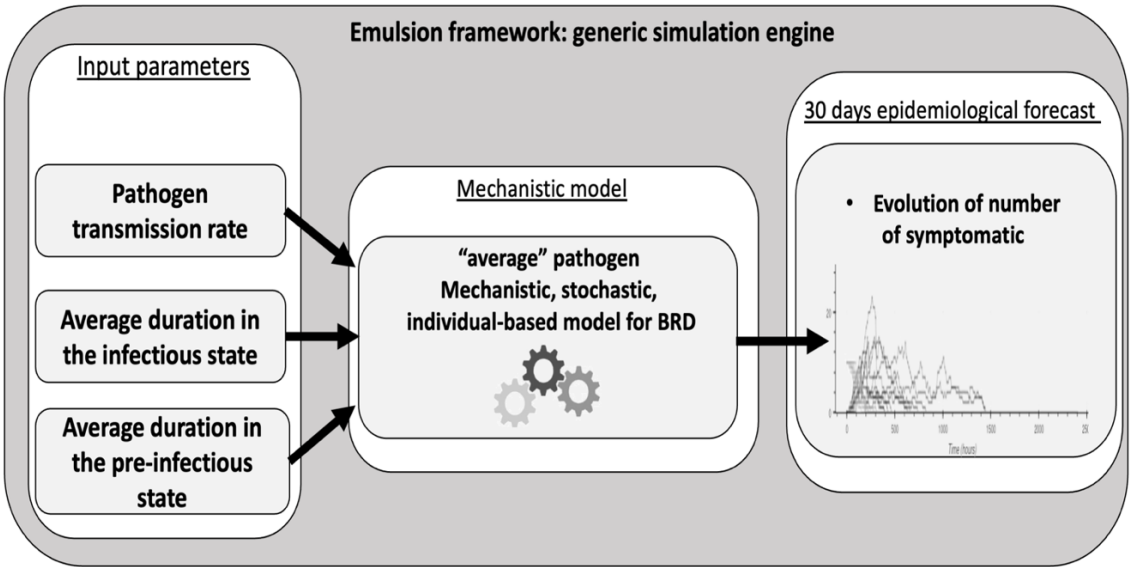

Figure 3. Simplified process of how the average pathogen model was used

Integrating a deep learning model with a mechanistic model: involves employing parameter inference, a computational approach used in various scientific disciplines to estimate the unknown parameters of a statistical model so that its predictions match, at best, observed data. The deep learning model predicts the clinical health state of an animal, distinguishing between symptomatic and asymptomatic states (Fig.4a). The total count of predicted diseased animals in a pen corresponds to the number of symptomatic animals. The average pathogen mechanistic model generates various outputs, only the count of symptomatic animals is considered (Fig.4b). Both the outputs of the deep learning model and the mechanistic model align, making parameter inference an ideal method to link two models, using deep learning predictions to estimate three parameters of the mechanistic model (Fig.4d), namely the pathogen transmission rate, the duration in infectious state and the duration in pre-infectious state.

The average pathogen model is categorized as an implicit generative model, capable of simulating samples however its likelihood is hardly obtainable. Hence, to estimate its parameters, a likelihood-free inference method, namely Approximate Bayesian Computation (ABC) (Beaumont, 2019) was employed. This involved sampling 10,000 parameter values within a biologically acceptable domain and using them to generate simulated datasets through the average pathogen model. Chosen summary statistics, in this case, the count of symptomatic animals, captured essential features of the observed data. The similarity between simulated and observed data was assessed using distances in their summary statistics the closest 1% of sampled simulated parameters were accepted. This process allowed for the estimation of the distribution of potential values for the chosen parameters. One extension of the ABC method was selected for this study, the ABC-NN (neural network), as it gave the most consistent results in our use cases.

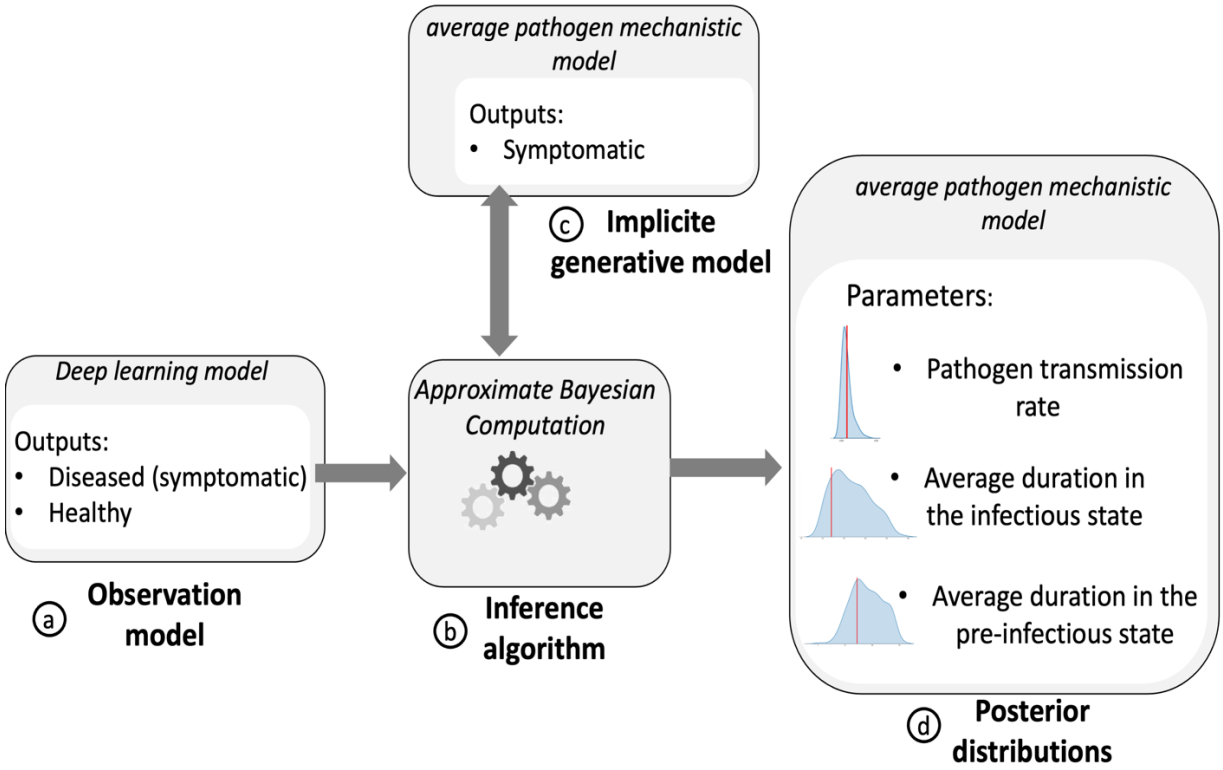

Figure 4. Method of coupling a deep learning model with a mechanistic model. Inference of the three biological parameters of an average pathogen BRD model

Evaluating the effectiveness of the inference method involved sampling values from the joint posterior distributions (Fig.4) and utilizing them to predict the number of symptomatic animals (also considered clinically diseased). This prediction was then compared to the actual number of detected diseased animals, using the mean absolute percentage error as the metric. The assessment of the inference method was carried out on two farms with different breeding practices, and the forecasting period was set at 30 days.

RESULTS

From Data to information: automatic diagnostics

Training the hybrid (CNN-RNN) deep learning architecture, using various spatial feature extractors demonstrated varying performance (Table 2.) due to their distinct architectural characteristics, including differences in structures and depth. VGG16 exhibited the poorest performance with a weighted F1-score of 14%, while InceptionV3 outperformed the rest with a weighted F1-score of 70%.

Table 2. Deep learning performance

Feature Extractor	Weighted Precision	Weighted Recall	Weighted F1-score	Accuracy
EfficientNetB7	0.67	0.62	0.63	0.62
InceptionResnetV2	0.71	0.50	0.49	0.50
InceptionV3	**0.72**	**0.69**	**0.70**	**0.69**
VGG16	0.09	0.31	0.14	0.31
InceptionV3 + InceptionResnetV2	0.71	0.62	0.63	0.62

In summary of the diagnostic phase, it is feasible to train a deep learning model using sensor data, particularly pulmonary ultrasound videos, to estimate the clinical health status of animals. However, it is important to note that the margin of error for the best model, when making predictions for 12 animals, is approximately $\pm$ 0.259 (or 25.9%) at a 95% confidence level. While the accuracy of the best model is reasonable considering it has been trained exclusively on ultrasound videos, using this model in real-life scenarios would result in an unacceptable margin of error.

From diagnostics to disease dynamic: prognostic

Due to the margin of error being too large for practical use on a farm with 12 animals, reliable data was used for the inference, specifically the ground truth. In Table 3 illustrates the estimated values of the three most critical biological parameters for two farms. The estimations are presented as the median, Q1, and Q3. Additionally, Table 3 includes the nominal values for these three parameters for comparison. In both farms, the estimated parameter values appear acceptable and closely align with the nominal values.

Table 3. Inferred value of parameters vs nominal value of parameters

Parameter name	Farm 1			Farm 2			Default model values
	Median	Q1	Q3	Median	Q1	Q3	calibrated
Pathogen Transmision rate	0.009	0.006	0.012	0.019	0.014	0.023	0.008
Mean duration in infectious	150	118	193	123	100	156	120
Mean duration in pre-infectious	87	68	115	76	58	100	72

Utilizing these estimated values, the number of animals considered asymptomatic over a 30-day period in both farms (Fig.5) was projected. The mechanistic model was run at discrete time steps, with each step occurring every 12 hours. For farm 1, the forecasted trajectory demonstrates an average error below 5%. However, for farm 2, the projected trajectory indicates an average error close to 23%.

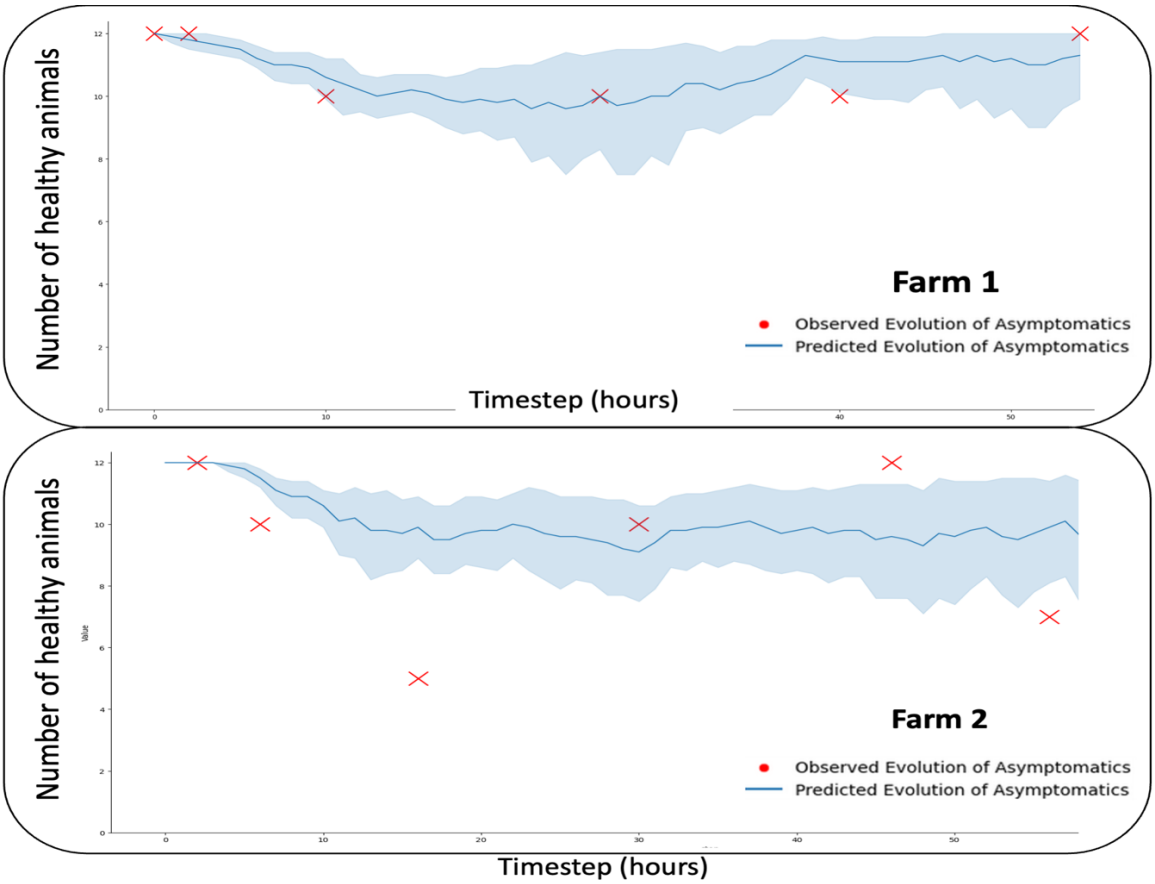

Figure 5. Asymptomatic forecast, ground truth vs calibrated average pathogen mechanistic model

In summary of the forecast phase, using clinical health status gives enough information to estimate the values of three crucial biological parameters: the pathogen transmission rate, the average duration in the infection state, and the average duration in the pre-infectious state. However, it is important to note that the average pathogen model is not suitable for every scenario.

DISCUSSION

This study demonstrated the feasibility of creating a hybrid approach that combines a deep learning model with a mechanistic model for diagnosing and predicting the dynamics of BRD. This adaptable approach can be implemented across various farms and scenarios, providing personalized diagnostics and predictions tailored to each farm's unique conditions. This has the potential to support the development of individualized control strategies and animal management practices based on specific farm circumstances.

However, it is important to acknowledge certain limitations in the proposed pipeline. Firstly, relying solely on pulmonary ultrasound videos as sensor data may not be sufficient to accurately estimate the clinical health status of each animal. This limitation arises because some symptoms caused by BRD, especially those affecting the upper respiratory tract, may not be visible in the lungs. Additionally, lung lesions become apparent only in the advanced stages of the disease. To address this issue, incorporating diverse sensor data, such as audio data already at our disposal, could be beneficial.

Secondly, the ground truth based on clinical symptoms may be more uncertain in detecting animals in the pre-infectious state. To tackle the challenge of a lack of a clear gold standard (Timsit et al., 2016) future research could explore the inclusion of biological exams, such as PCR and serological tests, which are presumed to provide more informative insights, especially regarding the type of pathogen infection.

Lastly, the average pathogen model may not be universally applicable, particularly in scenarios involving viral infections. In such cases, depending on the type of infectious agent, employing a pathogen-specific model (Sorin-Dupont et al., 2023) could enhance the accuracy of forecasting.

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Ethical approval concerning the French legislation on experimental animal care was approved by the Ethics Committee in Animal Experimentation in Oniris, Nantes, France (authorization on living animals No. CERVO-2022-7-V).

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