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"La connaissance s'acquiert par l'expérience, tout le reste n'est que de l'information".

- Albert Einstein (n.d.)

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Chapter 1

Introduction

1.1 Livestock farming, animal health and infectious diseases

Livestock farming today is embedded in a complex socio-economic landscape that underpins food security, rural development, and environmental sustainability. As global populations rise and resource constraints become more acute, the ability to produce high-quality animal products in a sustainable manner is more critical than ever. This sector not only ensures the availability of nutritious food but also supports the livelihoods of countless rural communities, thereby reinforcing local economies. In parallel, the modern challenges of animal health and public safety are converging, with infectious diseases emerging as a significant threat that jeopardizes both the productivity of farming systems and the broader public health framework. The traditional approach to livestock management, which often treats animal health in isolation, is increasingly being questioned in favour of a more integrated strategy that acknowledges the intricate links between animal welfare, human well-being, and environmental health.

In this context, infectious diseases are not merely biological phenomena but are embedded within the socio-economic fabric of livestock farming. Their impact reverberates through production losses, escalating veterinary expenses, and the overuse of antibiotics, which in turn contribute to public health concerns such as antimicrobial resistance. These challenges demand a rethinking of conventional control measures and underscore the urgency of developing sustainable farming practices that can adapt to both immediate crises and long-term environmental pressures. By embracing an integrated approach, the sector can transform these challenges into opportunities for innovation, leveraging advanced technologies and interdisciplinary strategies to enhance animal health, protect public well-being, and ensure the economic viability of farming systems for future generations.

This section provides a comprehensive overview of the socio-economic landscape that surrounds livestock farming, underscoring its importance for food security, public health, environmental management, and the integrated “One Welfare” approach. It section also highlights key challenges related to the impact of infectious diseases on livestock farming as well as conventional methods used to diagnose, manage, and prevent these diseases and their inherent limitations.

1.1.1 Socio-economical context and the stakes

Livestock Farming, animal health well-being

Livestock farming constitutes a cornerstone of global agriculture, underpinning food security and rural development while driving significant economic contributions worldwide (Fig 1.1). In Europe, the average livestock farm covers approximately 34 hectares and maintains a herd size of around 47 livestock units, a scale that reflects both intensive production and resource management practices [1]. Globally, the sector contributes up to 50% of the agricultural gross domestic product and supports the livelihoods and food security of nearly 1.3 billion people in developing countries, highlighting its critical role in sustaining rural economies [2, 3]

The environmental footprint of livestock farming is also considerable. Livestock production occupies nearly 75% of the agricultural land, underscoring its extensive spatial demands and the pressure it exerts on natural ecosystems [4]. High animal densities in confined feeding operations lead to substantial nutrient emissions, with studies reporting significant releases of nitrogen and phosphorus into the environment, thereby contributing to issues such as greenhouse gas emissions and water eutrophication [5, 6, 7]

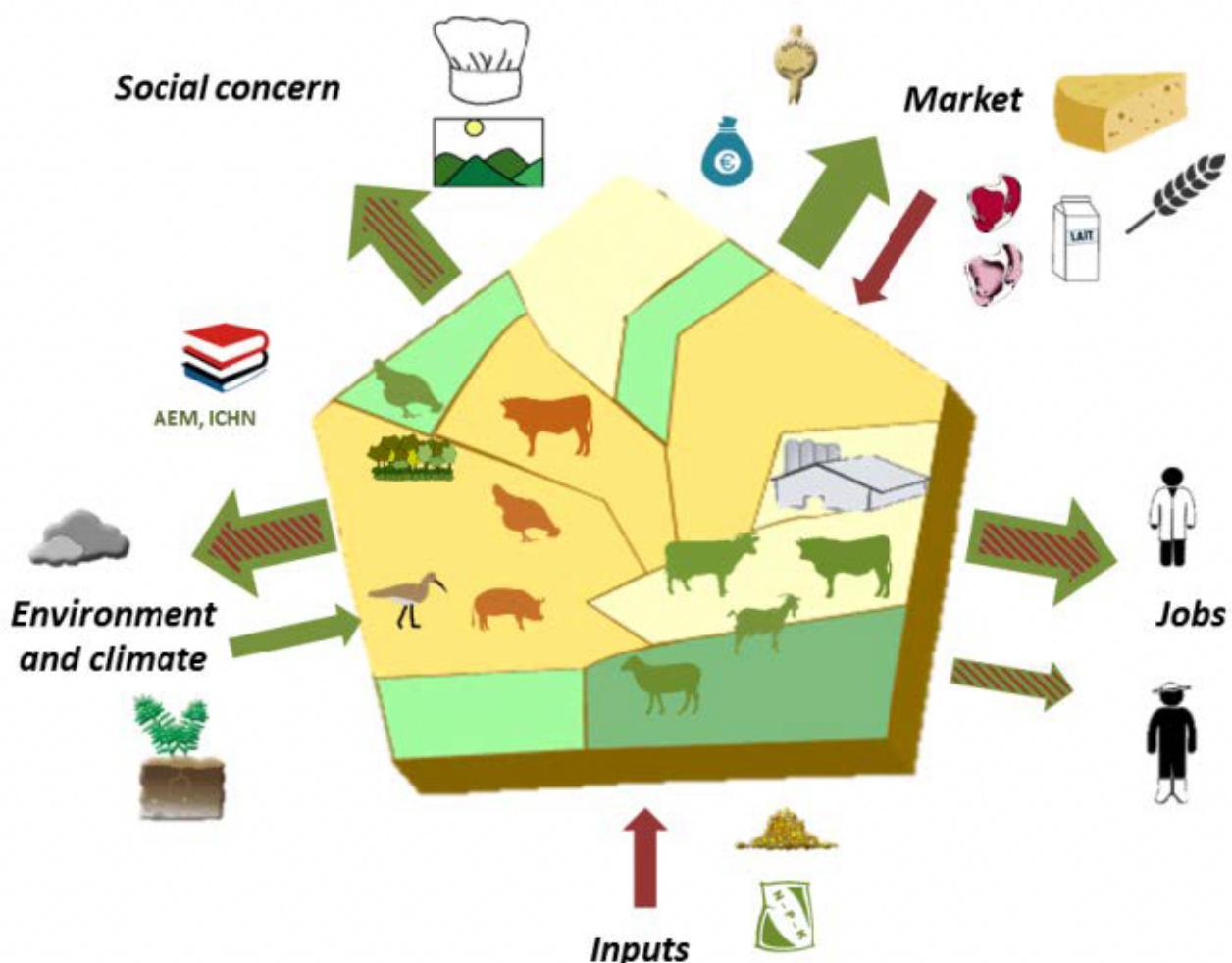


Figure 1.1: Bundle of services in areas with both crop and livestock farming. Illustration from [1]

Future projections indicate a continuing rise in global demand for animal products, a trend driven by the so-called "livestock revolution" that accompanies increasing incomes and population growth,

particularly in emerging economies [8]. This anticipated growth in demand is set against the backdrop of an already extensive current offer, where production scales and market dynamics are closely intertwined. Furthermore, livestock production accounts for about 15% of global greenhouse gas emissions, with ruminants being the primary contributors due to their lower feed conversion efficiencies [9]. These figures underscore the urgency of balancing the expanding demand with sustainable production practices that safeguard both environmental quality and public health.

Animal health and welfare remain central to the sustainability of livestock farming systems. Societal concerns over animal well-being are driven not only by ethical considerations but also by the direct links between robust animal health, food safety, and public health outcomes. Ensuring high standards of animal welfare enhances productivity by improving feed conversion efficiency and reducing culling rates, while also reinforcing consumer trust in the safety and quality of animal products [3].

One of the major pressures on livestock farming is infectious diseases. These diseases challenge animal health and welfare, threaten food security and public health, and raise ecological concerns. The following subsection provides a brief overview of infectious diseases, detailing their intricate relationship with the environment and their overall impact on livestock systems.

Livestock infectious diseases

Bernard Vallat, Director General of the World Organisation for Animal Health (OIE), emphasized the escalating challenges posed by infectious diseases by stating, “As a result of globalisation and climate change, we are currently facing an unprecedented worldwide impact of emerging and re-emerging animal diseases and zoonoses (animal diseases transmissible to humans)” [10]. Indeed, infectious diseases represent a significant threat to livestock farming, deeply intertwined with environmental, economic, and public health factors. These diseases are caused by pathogenic microorganisms including bacteria, viruses, fungi, and parasites, capable of spreading directly or indirectly among animals, across species barriers (zoonoses), or through contaminated environmental media such as soil, water, or feed. Infectious disease has been chosen for consideration because globally these diseases have historically been, continue to be, and are expected to remain major concerns in the future. The increasing intensification of modern animal husbandry has encouraged the proliferation of infectious diseases and resulted in the emergence and increased importance of so-called multifactorial diseases.

Within livestock systems, infectious diseases manifest in diverse forms and can be categorized by their clinical presentations and modes of transmission. Respiratory infectious diseases, notably bovine respiratory disease complex and contagious bovine pleuropneumonia, pose substantial threats due to their rapid spread and significant economic impacts. Gastrointestinal infections such as salmonellosis and coccidiosis critically impair animal health and productivity through severe digestive disruptions. Bloodstream infections, exemplified by African swine fever, are particularly devastating due to their rapid progression, high mortality rates, and significant implications for international trade. Vector-borne diseases like bluetongue, transmitted by biting midges, are increasingly problematic in regions experiencing climate change, altering vector habitats and expanding disease ranges. Skin infections, including dermatophytosis and footrot, impose chronic health and welfare issues, severely affecting productivity and animal product quality [11]

The economic repercussions of infectious diseases in livestock are substantial, with diseases such as African swine fever and bovine tuberculosis significantly reducing productivity and incurring considerable veterinary costs [11]. Moreover, globalization, climate variability, and intensive farming practices further facilitate pathogen proliferation and dissemination, amplifying the scale and

severity of outbreaks. Historical translocation events have dramatically demonstrated this potential, with diseases such as rinderpest and foot-and-mouth disease causing severe disruptions to global livestock production and trade [12]. Additionally, the widespread emergence of antibiotic resistance, driven by excessive antibiotic use in animal agriculture, poses critical challenges to effective disease management, raising serious concerns for animal welfare and health due to therapeutic failures [13]. To mitigate these threats, conventional control measures have and still play a role, which are explored in the following subsection.

1.1.2 Conventional control strategies of infectious diseases

Conventional control strategies for managing infectious diseases in livestock primarily rely on accurate diagnosis and prognosis to mitigate outbreaks and prevent their spread. Diagnosis involves identifying diseases through clinical appraisal, visual and tactile assessments conducted by farmers and veterinarians—and biological examinations, including laboratory analyses like PCR tests on collected samples. Prognosis entails predicting the potential progression and impact of identified diseases based on expert knowledge, historical data, and empirical observations. These methods culminate in tailored control recommendations, such as vaccination, quarantine, biosecurity protocols, and prudent use of antimicrobials. Given that livestock farming heavily utilizes natural resources, it is imperative to raise animals using best practices and innovations aimed at producing more with fewer inputs, including reduced use of water, land, feed, antibiotics, and waste. Livestock effluents, rich in organic matter, nutrients, pharmaceuticals, and heavy metals—can negatively affect ecosystems by contaminating soil and water bodies, accelerating eutrophication, and fostering antibiotic-resistant bacteria [14, 15, 16, 17]. Consequently, effective conventional disease control strategies are vital not only for animal welfare but also for preserving environmental health and public safety.

Despite their widespread adoption, conventional control methods possess inherent limitations, presenting significant challenges in practical livestock management. Clinical appraisal, although efficient and quick, is notably subjective and prone to inconsistencies between observers. Biological examinations, despite their precision, often introduce substantial delays and costs, rendering them less suitable for rapid decision-making during acute outbreaks. Scalability becomes problematic as livestock farming intensifies, with large-scale epidemiological surveillance demanding substantial human, financial, and logistical resources. The COVID-19 pandemic has starkly illustrated the importance of proactive risk management in infectious disease outbreaks, highlighting the necessity to better understand the mechanisms that influence disease emergence and severity. In parallel, broader societal debates challenge the sustainability of current livestock production practices, questioning the dominant productivist model and encouraging transitions toward more sustainable and integrative frameworks such as "ecological intensification," precision livestock farming utilizing transmitters, robotics, and statistical analyses, and agroecology, which relies on ecosystem services. These approaches aim to reconcile productivity demands with the critical need to manage environmental impacts responsibly [1]. Consequently, there is a growing urgency to adopt automated, and integrative methodologies capable of overcoming the complexities inherent in infectious disease management, an area where precision artificial intelligence, epidemiology and data science could offer promising avenues for innovation and sustainability.

1.2 Artificial intelligence, epidemiology and data science

Artificial Intelligence (AI) is the study of computer systems designed to perceive their surroundings, think logically, learn from experiences, and take appropriate actions, essentially mimicking or enhancing human intelligence [18]. Over time, AI has changed significantly. Early approaches focused on logic-based systems that relied heavily on explicit rules [19]. Today, AI also uses machine learning, a method where algorithms automatically discover patterns directly from large amounts of observations [20].

Epidemiology is the study of how diseases spread in populations, what causes them, and how they can be controlled. A central idea in both epidemiology and AI is modelling. Modelling means creating simplified mathematical or computational representations of complex real-world phenomena to better understand, predict, and manage them. In epidemiology, models help scientists describe how diseases spread, predict how outbreaks might evolve, and guide effective public health responses [21].

Regardless of the chosen modelling approach, the initial step always involves allowing the model to accurately perceive and interact with its environment. In livestock farming, this essential step is achieved through the use of sensors. These sensors can track animal behaviour, physiological parameters, location, and environmental conditions, enabling continuous monitoring of animal health and facilitating the early detection of diseases [22]. Sensor-derived data can then feed into various modelling methods used in artificial intelligence to support decision-making. In this thesis, we particularly focus on two modelling paradigms: epidemiological mechanistic models, which rely on detailed knowledge of disease dynamics, and deep learning models, which automatically learn complex patterns directly from sensor data.

1.2.1 Precision livestock farming: sensors and observations

Precision livestock farming (PLF) represents a technological shift aimed at improving livestock management by continuously monitoring animal health, welfare, and productivity through automated sensor systems. Driven by economic pressures, livestock farms have increasingly scaled up, leading to challenges in maintaining close and accurate animal monitoring through traditional methods. Consequently, PLF technologies have become integral for bridging the widening gap between animals and farmers [23].

The integration of sensor technology into livestock farming encompasses several categories. Behavioural sensors, such as accelerometers and video tracking systems, enable continuous and objective measurement of animal activities including movement, resting patterns, and feeding behaviours. These sensors assist in detecting behavioural deviations, indicative of underlying health issues, stress, or welfare concerns [24, 25, 26]. Positional sensors, like Real-Time Locating Systems (RTLS), provide precise animal location data, useful for interpreting individual and group dynamics within the herd [27].

Biological sensors include devices such as ruminal boluses, ear tags, or collars equipped with sensors to measure physiological parameters including body temperature, rumination, and hormone levels, essential for early detection of conditions such as respiratory disorders and reproductive events [28, 29]. These sensors offer considerable accuracy and can significantly surpass human observation efficiency, with heat detection sensitivities ranging from 60–100% compared to 50–60% through visual observation alone [29].

Environmental sensors monitor conditions inside livestock facilities, such as temperature, hu-



Figure 1.2: Illustration of the diverse categories of observations in livestock farming

midity, air quality, and gas concentrations. These factors significantly impact animal productivity and health, particularly in intensive farming systems, and accurate environmental data facilitates proactive management interventions [30, 31]. Operational sensors additionally track management practices, feed intake, water use, and equipment status, further enriching the database required for effective decision-making in livestock management [32, 33]. Sound analysis represents another significant innovation in PLF, notably for the early detection of respiratory infections in pigs, providing alerts up to two weeks earlier than traditional veterinarian observations [34]. Similarly, image analysis technologies are being actively deployed to monitor behavioural interactions, with promising results demonstrated in pig aggression detection using advanced algorithmic identification of specific aggressive markers such as head-to-head knocking and ear biting [25].

Despite the proliferation of sensor-based technologies, their adoption rates vary widely among different livestock production types. Surveys conducted in France, for example, indicated that about 10% of farms were equipped with automated milk meters by 2014, and an additional 13% had adopted robotic milking systems, highlighting a significant and growing acceptance of these particular sensor technologies in dairy farming [35].

This rich, high-throughput data collection which could allow us get an holistic overview of environment and animals (Fig 1.2) is not an end in itself but serves as the foundation for advanced modelling techniques. Once the observations are collected, the extraction of insights through various modelling approaches becomes essential for transforming raw data into actionable knowledge. In the subsequent section, we will explore epidemiological mechanistic models that utilize this sensor-derived information to predict disease dynamics and guide decision-making in livestock management.

1.2.2 Epidemiological modelling: Stochastic mechanistic models

Mechanistic models in epidemiology have played a central role in translating complex, interdisciplinary insights into quantitative frameworks that inform evidence-based policy-making. Their construction begins by segmenting the population into compartments, typically susceptible, infected, and recovered, following seminal work by Bernoulli (1760), Ross (1916), and Kermack and McKendrick (1927) as detailed in early epidemiological studies. These foundational models not only formalized the understanding of disease transmission dynamics through systems of differential equations but also provided a platform for incorporating additional layers of biological, economic, and social theory into rule-based algorithms.

Building on these early models, researchers have developed increasingly sophisticated mechanistic models that integrate heterogeneous mixing patterns, demographic processes, and spatial structures. In the context of livestock infectious diseases, for instance, models have been extended to capture multi-scale interactions—from within-host processes to regional spread, thereby enabling the simulation of targeted interventions such as vaccination and movement restrictions [36, 37]. The ability to embed theoretical insights into mathematical formulations allows these models to explore scenarios that are otherwise ethically or logically infeasible to observe directly. This is crucial for policy-making, as it offers decision-makers evidence-based insights into the potential impacts of various control measures on both disease spread and animal welfare [38, 39].

The construction of these models generally involves formulating a set of differential equations or stochastic processes that describe transitions between defined compartments. Parameters such as the transmission rate, recovery rate, and contact structure are estimated using empirical data through methods like maximum likelihood estimation or Bayesian inference [40, 41]. These fitting procedures are critical to ensure that the model outputs faithfully represent the underlying biological processes. However, a significant challenge arises from the increasing use of sensor-based data in modern epidemiological studies. Unstructured datasets, such as video and audio recordings from precision livestock farming, are rich in information yet notoriously difficult to process and integrate into these models due to the labour-intensive nature of manual data curation. The relevance of the model only depends on its use and the available data/knowledge to build and parametrize it.

While preliminary efforts have begun to explore deep learning techniques for handling such unstructured data, the primary strength of mechanistic models lies in their capacity to consolidate interdisciplinary theoretical knowledge into a structured, predictive framework. This integration not only supports the evaluation of control strategies under diverse scenarios but also provides a safe, ethical alternative to field experimentation by simulating conditions that are hard to replicate in reality.

1.2.3 Machine learning modelling: classical deep learning models

Machine learning is an integral subfield of artificial intelligence that focuses on automatically deriving predictive models directly from datasets rather than embedding knowledge via mechanistic, rule-based models such as those used in traditional epidemiology. In essence, it's like teaching a child to recognize a cat by showing hundreds of pictures rather than providing explicit instructions [42]. At its core, deep learning creates multi-layered models that learn by adjusting their internal parameters based on examples. For instance, in image recognition, the first layers may detect simple features like edges and colours, while later layers combine these features to identify more complex patterns, such as the specific contours and textures that form a cat's face [20]. Early work in this area started with simple rule-based systems and perceptron models [42] and evolved over the decades

into architectures that can span 10 to over 100 layers with tens to hundreds of millions of parameters [20]. These deep models function as universal approximators, capable of modelling highly non-linear relationships by iteratively minimizing prediction error through back-propagation [43] and stochastic gradient descent techniques that adjust millions of weights over thousands to millions of iterations using mini-batches of 32–512 samples [44].

Among the classical deep learning models, several architectures have been particularly influential. Feed-forward neural networks serve as the basic building blocks in which data flows in one direction from input to output. Convolutional neural networks have revolutionized computer vision by applying convolutional filters and max pooling operations to extract spatial hierarchies from high-resolution images (often 512×512 pixels or larger) and achieve translational invariance [45, 46]. Recurrent neural networks, and particularly their long short-term memory variants, are engineered to handle sequential data by overcoming issues like the vanishing gradient problem through gating mechanisms, thus capturing dependencies that span thousands of time steps [47, 48]. More recently, graph neural networks have emerged to model data with non-Euclidean structures—such as relationships in social networks or complex interactions on a farm [49], while transformer models leverage self-attention mechanisms to process entire sequences in parallel, which improves the modelling of long-range dependencies and reduces training time [50]. In addition to these traditional architectures, foundational models—particularly large language models such as GPT (generative pre-trained transformer) have revolutionized natural language processing by being trained on vast amounts of text data to predict and generate human-like language [51]. However, a significant challenge for these models is “hallucination,” where they generate plausible-sounding but factually incorrect or nonsensical outputs. This occurs because these models rely on statistical patterns rather than deep, mechanistic understanding, lacking strong theoretical grounding in the underlying principles of language [52, 53]. In contexts like livestock management, where deep learning applications in natural language processing are used to analyse veterinary reports and sensor logs, such hallucinations can lead to false positive and incorrect diagnoses or misguided recommendations, highlighting the need for integrating explicit domain knowledge to improve reliability.

Because these deep learning models can have millions of parameters and many layers, they are often described as “black boxes” systems that deliver high accuracy yet offer little insight into how decisions are made. This opacity is problematic, especially in high-stakes domains such as health-care, autonomous driving, or livestock management, where understanding a model’s rationale is crucial for safety and trust [54]. Explainable Artificial Intelligence (XAI) addresses this gap by providing methods to interpret and understand the internal workings of complex models. For example, Gradient-weighted Class Activation Mapping (Grad-CAM) generates visual maps that indicate which parts of an image were most influential for the model’s decision, and Local Interpretable Model-agnostic Explanations (LIME) approximate a deep model’s local behaviour with a simpler, interpretable model for specific instances [55, 56]. Another critical component is uncertainty quantification, which ensures that a model not only provides a prediction but also a measure of confidence in that prediction. Bayesian Neural Networks use variational methods to assign probability distributions to model parameters, so instead of providing a single fixed output, the network indicates, for example, that it is 90% confident that an image contains a cat, with the remaining 10% reflecting uncertainty [57]. Similarly, conformal prediction techniques provide statistically valid prediction sets, ensuring that the true outcome is contained within these sets at a pre-defined confidence level [58].

Transformer-based models have been deployed to automatically analyse veterinary clinical records, social media posts from farmers, and sensor-generated text logs to identify early signs of disease outbreaks or stress in livestock populations. Deep learning models have also been used to monitor animal behaviour through video analysis, allowing for the detection of anomalies such as lameness

or aggressive behaviour, thereby enabling timely interventions that improve animal welfare and productivity [59]. Other studies have demonstrated the utility of deep learning in livestock management by combining image analysis with sensor data. For example, CNNs have been used to automatically count and classify animals in large herds, while natural language processing helps in summarizing and integrating textual data from various reports, creating a comprehensive monitoring system that can alert farmers to potential issues before they escalate [60].

All these techniques, deep neural architectures and its security techniques such as XAI methods and uncertainty quantification tools, come together to form a more robust and transparent system. By explaining their inner workings and providing confidence measures, these methods help users understand not only what the model’s decision is, but also why it made that decision and how reliable that decision is. This comprehensive approach is especially important in fields where decisions have significant consequences, such as in medical diagnosis, financial forecasting, or autonomous driving [44, 54]. Without integrating additional domain-specific knowledge, these models can struggle to generalize beyond the data on which they were trained, leaving significant opportunities for further research at the intersection of deep learning and mechanistic modelling.

1.2.4 Hybrid modelling: machine learning and epidemiological models

Recent research in infectious disease modelling has sought to address the well-known limitations of data-driven and theoretical approaches when used in isolation. Deep learning methods, while highly effective at capturing complex, non-linear patterns from structured data, often struggle to extrapolate when confronted with untrained or sparse data. In contrast, mechanistic epidemiological models, which are built upon established theoretical principles of disease dynamics, frequently face challenges when fitting unstructured observations. This has led to the development of several hybrid integration approaches that aim to merge the complementary strengths of both methodologies to achieve objectives such as forecasting, model parametrization and calibration, intervention assessment and optimization, retrospective epidemic course analysis, transmission inference, and outbreak detection [61].

One prominent integration approach involves using Physics-Informed Neural Networks (PINNs) and Epidemiology-Augmented Artificial Models (EAAMs) to learn unknown components of epidemiological models. In these methods, deep learning architectures are augmented by incorporating epidemiological principles directly into the network—often through residual loss terms—to learn hidden state variables, parameters, or derivatives. This approach helps model parametrization and calibration while also improving forecasting capabilities by enforcing consistency with known epidemic dynamics. Studies employing this method have demonstrated its effectiveness on both real and synthetic datasets, as documented in recent literature [62, 63, 64, 65, 66, 67, 68, 69, 70] for PINNs; [71, 74, 75, 76, 77, 78, 79, 80, 81, 72, 73] for EAAMs

Another strategy leverages mechanistic models to generate synthetic datasets under varied parameter conditions. Deep learning architectures, such as recurrent neural networks, are then trained on these synthetic datasets to predict unobserved model components or forecast future epidemic trajectories. By doing so, this approach addresses the challenge of limited real-world data and contributes significantly to both forecasting and transmission inference. The synthetic data enable the model to generalize beyond the training domain, thereby enhancing its capacity to infer underlying transmission patterns in scenarios where observational data are sparse [82, 93, 104, 113, 114, 115, 116, 117, 118, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 94, 95, 96, 97, 98, 99, 100, 101, 102, 103, 105, 106, 107, 108, 109, 110, 111, 112]

A further integration approach embeds epidemiological constraints directly within deep learn-

ing frameworks. By incorporating established conservation laws or differential equations into the model's inputs, loss functions, or architecture, these hybrid models ensure that predictions adhere to the theoretical underpinnings of disease dynamics. This method improves both the accuracy of forecasts and the robustness of retrospective epidemic course analyses by aligning data-driven predictions with fundamental epidemiological knowledge [62, 63, 64, 65, 66, 67, 68, 69, 70]. In a related vein, reinforcement learning and optimal control frameworks have been integrated into simulation environments derived from mechanistic models. In these approaches, reinforcement learning agents interact with epidemiologically informed simulations to iteratively optimize intervention strategies. This methodology directly addresses the objective of disease intervention assessment and optimization by enabling the exploration of optimal control policies through continuous feedback from the simulation environment [119, 130, 141, 151, 152, 153, 154, 155, 156, 120, 121, 122, 123, 124, 125, 126, 127, 128, 129, 131, 132, 133, 134, 135, 136, 137, 138, 139, 140, 142, 143, 144, 145, 146, 147, 148, 149, 150] for RL methods and [157, 125, 158, 159, 160, 161] for optimal control frameworks.

Additional integration strategies focus on enhancing the quality of unstructured observational data and reducing prediction error. Techniques such as support vector machines and tree-based classifiers are applied to extract auxiliary information from heterogeneous datasets, thereby refining parameter estimation and indirectly supporting retrospective analysis and outbreak detection. Moreover, ensemble modelling methods, which combine outputs from independently trained models through stacking, boosting, or bagging, have been shown to reduce overall prediction error and increase robustness. These ensemble techniques facilitate improved forecasting accuracy and more reliable outbreak detection by synthesizing diverse model predictions [162, 163, 164, 165] and [166, 167, 168, 169, 170, 171]. Complementing these methods, Bayesian neural networks have been employed to quantify uncertainty in parameter inference. By approximating the posterior distribution of model parameters, this approach provides critical measures of confidence that enhance forecasting, transmission inference, and outbreak detection [172, 173, 174, 175]. Finally, clustering-based decomposition uses unsupervised learning algorithms, such as k-means, to partition large-scale epidemiological models into smaller sub-models. This segmentation enables localized analysis and tailored intervention strategies, thereby strengthening retrospective epidemic course analysis and improving the sensitivity of outbreak detection [176].

Among the studies reviewed, a total of 26 infectious diseases were investigated using integrated models. Notably, COVID-19 dominated the research landscape, accounting for 60% of the studies, with 148 investigations dedicated to this disease. Influenza was the focus in 7% of the studies, dengue in 2%, and HIV in 1%. In addition, 23% of the studies utilised hypothetical disease scenarios to demonstrate the applicability of the methods. Based on the reviewed studies, there isn't strong evidence that sensor observations—such as data directly collected from IoT devices or on-farm sensors—have been prominently integrated into these frameworks. Some work has explored the use of sensor-based data like satellite imagery (which is one form of sensor observation) to capture environmental factors. However, most approaches in the review primarily rely on traditional surveillance data and non-traditional sources such as social media, search queries, or emergency reports, rather than sensor observations from livestock or similar settings. This represents an opportunity for future research to incorporate direct sensor data for automated monitoring and relevant context-specific insights.

1.3 Thesis objective and outline

1.3.1 Towards an innovative and AI-based methodology for controlling infectious disease in livestock farming from sensor observations

Managing and controlling infectious animal diseases within livestock farming involves understanding and intervening within a highly complex system. This complexity arises from intrinsic parameters—such as pathogen strains and specific farming practices, as well as extrinsic parameters, notably detection and control measures, which are inherently variable over time. Compared to conventional control strategies, artificial intelligence (AI) has emerged as a particularly promising approach for conceptualizing epidemic dynamics, modelling their progression, and anticipating their evolution through simulations [177]. Such simulations enable, at minimum, the evaluation and comparison of various disease management scenarios, and facilitate the creation of decision-support tools (DSTs) developed collaboratively with stakeholders such as farmers, veterinarians, animal science specialists, and public decision-makers [38].

The current period of agricultural digitalization further strengthens the integration of stakeholders with these DSTs, particularly through the emergence of AI-driven tools capable of constructing zootechnical descriptors that traditionally represented a significant manual workload for farm operators. Within the broader scope of precision agriculture, there has been significant development and deployment of sensor technologies designed to continuously monitor physiological variables at the individual animal scale, as well as environmental conditions at the farm level. These sensors aim to generate short-term alerts (on the order of hours or days) related to critical stages of animal life cycles (such as parturition or oestrus), animal welfare, and even, in crop farming contexts, risks associated with weather conditions (thermal or hydric stress) or ecological threats like pest invasions [178].

Nevertheless, particularly in animal health contexts concerning infectious diseases, sensor-generated alerts tend to lack specificity, resulting in a high incidence of false positives. Such false alarms impose substantial cognitive burdens on farm operators, who consequently either disregard these alerts due to their perceived irrelevance or initiate unnecessary and excessive interventions. Hence, designing innovative methodologies that, despite the inherent lack of specificity in sensor alerts, can provide precise and actionable recommendations over longer and more human-compatible planning horizons (spanning several days or weeks), remains an open research question. It is precisely this unresolved challenge that this thesis seeks to address.

Consequently, the core research question guiding this thesis is: "How can sensor observations be effectively employed to study infectious diseases and support informed decision-making?"

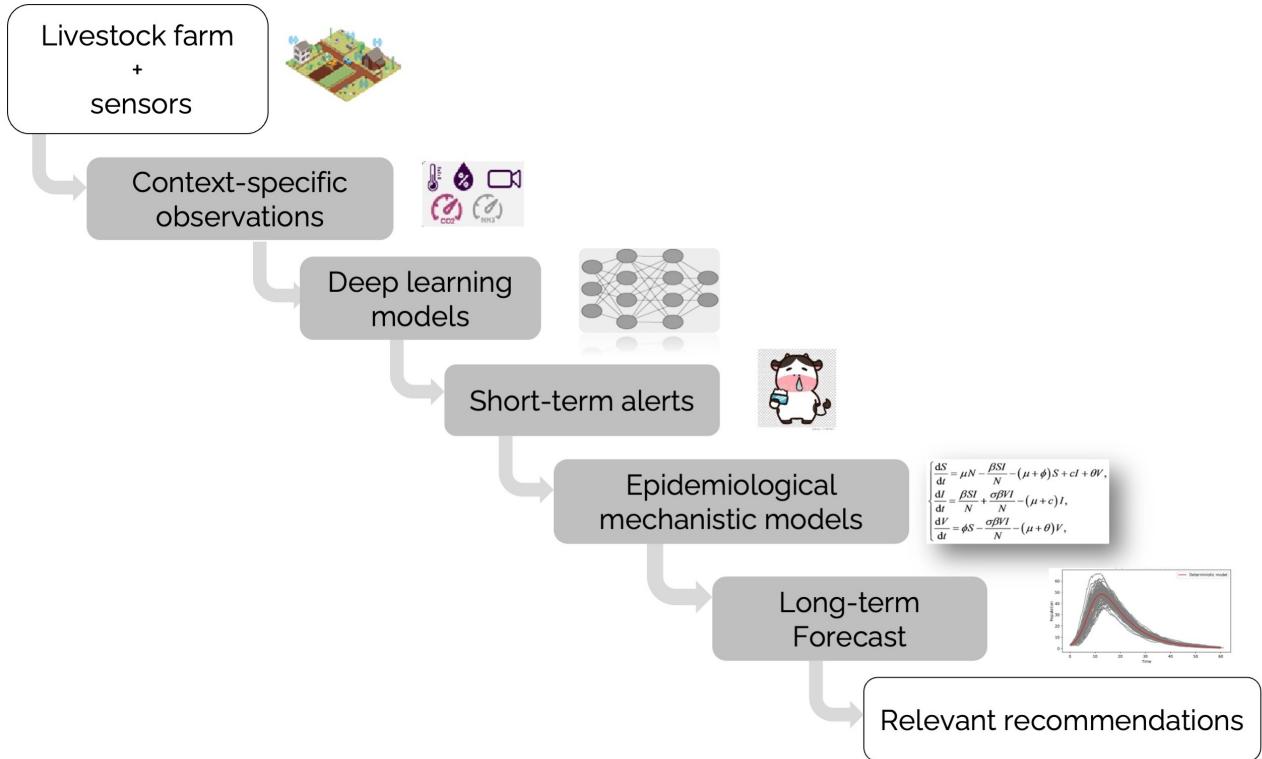


Figure 1.3: How can sensor observations be effectively employed to study infectious diseases and support informed decision-making?

Our primary hypothesis (Fig 1.3) posits that the optimal scientific approach to address contemporary quantitative challenges in animal health involves the integration of diverse artificial intelligence methodologies. In this thesis, we explore the complementarity between deep learning models and mechanistic epidemiological models. This integrative strategy leverages the extensive representation capabilities, multi-level analysis, and interdisciplinary expressivity of mechanistic epidemiological models while capitalizing on deep learning's robust data-mining capabilities. This fusion aims to achieve better integration of real-world observational data (derived from sensors, farmers, and veterinarians) with disease predictions across multiple temporal scales—ranging from short-term (days) to medium and long-term (weeks or months).

1.3.2 Use-case: Bovine Respiratory Diseases in young beef cattle sector

Bovine Respiratory Disease (BRD) represents the foremost animal health concern in cattle feedlots, negatively impacting animal welfare, economic performance, and public health through excessive antimicrobial use [178]. BRD significantly reduces animal growth rates and productivity, resulting in increased veterinary and medicinal expenses, as well as higher mortality rates—averaging approximately 3% [179]. It is also the primary reason antibiotics are administered in cattle production, affecting roughly 20% of fattening cattle [180].

The aetiology of BRD is multifactorial (fig 1.4), arising from complex interactions among intrinsic and extrinsic factors. Intrinsically, animal susceptibility is influenced by breed, immunity, and simultaneous infection by multiple pathogens, notably *Mannheimia haemolytica*, *Pasteurella multocida*, and Bovine Respiratory Syncytial Virus (BRSV), whose interactions are not yet fully understood [181, 182]. Extrinsic risk factors—such as stressful transportation conditions, herd density, feed management, housing conditions, biosecurity protocols, and climatic conditions—also strongly influence

disease occurrence and severity. Together, these intrinsic and extrinsic complexities severely limit the reliability of BRD prognosis, control strategies, and disease modelling.

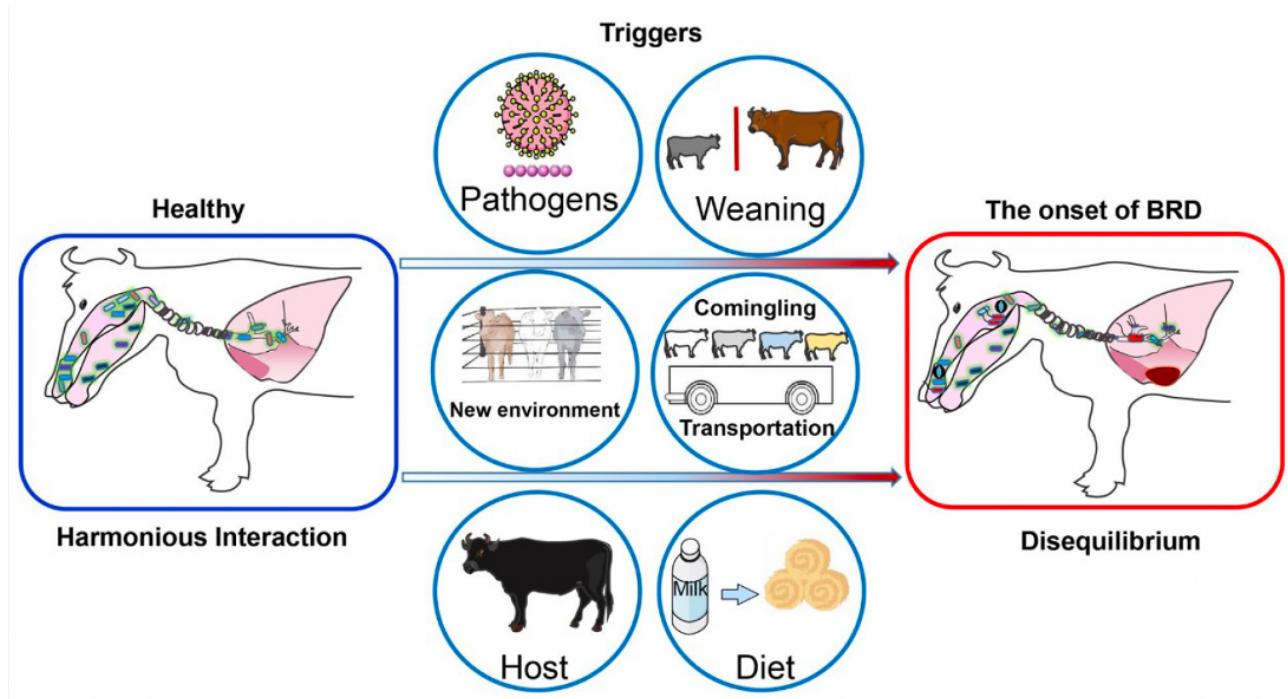


Figure 1.4: BRD etiology. From Jio-anmin et al., 2022. Burden in animal welfare, antimicrobial use and economic costs.

Diagnosing BRD is particularly challenging due to non-specific clinical presentations such as cough, nasal discharge, hyperthermia, anorexia, lethargy, and impaired growth—symptoms overlapping with many other diseases [181, 183]. Traditional visual detection based on behavioural appraisal is limited, displaying low sensitivity (62%) and specificity (approximately 63%), thereby resulting in frequent misdiagnoses (false positives) or delays in detection [184, 185]. Moreover, cattle often mask early clinical symptoms due to inherent prey behaviour, complicating timely and accurate identification of infected animals [183]. Additionally, limited veterinary expertise in rural areas of France further exacerbates accurate detection.

Recent advances in precision livestock farming [186, 187] have enabled continuous monitoring of animal health through sensor technologies such as accelerometers, microphones, thermometers, and cameras, measuring bio-signals indicative of BRD (e.g., body temperature, behavioural patterns, and respiratory sounds) [188]. Timsit et al. (2011) previously demonstrated that about 73% of hyperthermia episodes were associated with BRD, suggesting temperature-based monitoring's potential diagnostic utility [189]. More recently, Concorde et al. (2022) developed logistic regression models using sensor data (collar, pedometer, intra-ruminal bolus), achieving sensitivity and specificity rates of approximately 75% and 76%, respectively, capable of predicting BRD clinical signs up to 24 hours in advance [190]. Similarly, Ramezani et al. (2022) evaluated accelerometer-based ear-tag sensors detecting behavioural changes (activity, inactivity, rumination), demonstrating significant differences between healthy and diseased calves, although further validation in larger cohorts remains necessary [191].

Despite promising early detection results, most sensor-based studies remain limited by reliance on traditional machine learning models incapable of robust forecasting, hindering their predictive utility for scenarios that differ significantly from observed data. This limitation restricts their capacity to support evidence-based management and informed control interventions effectively, as complete observation of BRD dynamics in field conditions is ethically and practically unfeasible.

One study even proposed that further studies with higher number of diseased animals are necessary to improve their performance.

Complementary to sensor-based approaches, mechanistic epidemiological modelling has emerged as a promising solution to overcome observational limitations. Picault et al. (2022) [192] conducted an *in silico* modelling study identifying potential sensor-based management strategies. However, these mechanistic models were primarily calibrated from existing veterinary literature rather than empirical sensor data, resulting in uncertainties regarding their practical and explanatory utility in real-world veterinary scenarios. Furthermore, such modelling often involves invasive and expensive sensor technologies, underscoring the necessity of exploring alternative, non-invasive, cost-effective sensor modalities (e.g., audio, video, image analysis) for broader deployment.

Addressing these critical limitations, this thesis, collaboratively developed by INRAE, Adventiel, and myself :), seeks to develop innovative artificial intelligence methodologies specifically tailored for BRD diagnostics and prognostics, yet adaptable to other livestock or plant epidemiological contexts. By integrating deep learning with mechanistic epidemiological modelling, this work explicitly aims to enhance the interpretability, accuracy, and predictive robustness of sensor-derived observations (see Fig 1.3). The resulting methodologies aims to minimize inappropriate antimicrobial usage, improve animal welfare, reduce economic losses, and support long-term, evidence-based decision-making in precision livestock farming.

1.3.3 Originality of this thesis

A synergy of interdisciplinarity expertise

This doctoral project is structured under the CIFRE program ("Convention Industrielle de Formation par la Recherche"), an initiative established in France to foster collaboration between doctoral candidates, companies, and public research laboratories. The CIFRE framework encourages strong public-private partnerships, facilitating innovation that combines academic rigor with practical industry relevance.

In this thesis, such synergy is specifically realized through collaboration among distinct but complementary entities: Adventiel, INRAE (the French National Research Institute for Agriculture, Food, and Environment). Adventiel is a French company that specializes in digital solutions tailored specifically for the agricultural and agri-food sectors, providing services ranging from application development and artificial intelligence solutions to data science, software hosting, and comprehensive IT management. Their expertise and technological infrastructure, including advanced server configurations and data storage solutions, have substantially supported data collection and analysis during this research.

Complementarily, INRAE represents a world-leading public research institution dedicated to addressing critical global challenges such as climate change, biodiversity loss, and food security through the generation of scientific knowledge and innovation. INRAE's methodological approach emphasizes the integration of scientific insights from both animal and plant health domains. Indeed, one of INRAE's strategic research priorities has been to bridge methodological advances between these domains, a vision directly aligned with Adventiel's expanding R&D activities. Leveraging this diverse expertise, the thesis incorporates critical methodological advances from each partner. From INRAE, particularly via the DYNAMO team within the BIOEPAR unit, this thesis benefits from the EMULSION framework. EMULSION [193], is an innovative modelling tool combining knowledge representation and multi-agent systems to construct specialized epidemiological models. It in-

cludes a domain-specific language (DSL) tailored specifically for epidemiological modelling, which significantly facilitates interactions among interdisciplinary teams of biologists, veterinarians, and economists. Throughout this research, EMULSION's flexible and intuitive design greatly simplified adapting complex mechanistic models, enabling focused modifications even without extensive computational knowledge. Further, the BIOEPAR unit provided a solid foundational expertise in veterinary, epidemiological, immunological, and socio-economic aspects specifically related to bovine respiratory diseases (BRD). This included for instance the first mechanistic model developed for BRD within EMULSION, which served as a baseline for addressing key scientific questions in the present research.

In parallel, Adventiel contributed its extensive experience in developing deep learning solutions based on diverse data modalities (images, videos, and acoustic signals), aimed explicitly at creating indicators of animal welfare. Confidential deep learning architectures previously designed by Adventiel to analyse animal behaviour in video footage and detect anomalies in acoustic data provided methodological starting points. Additionally, Adventiel supplied essential hardware infrastructure and data management systems, which significantly streamlined data acquisition and analysis tasks throughout the thesis.

Finally, expertise from the Démécologie team of the IGEPP unit (INRAE) enriched the research by providing advanced statistical methodologies suited for inverse modelling, uncertainty quantification, and Bayesian inference. These methods are designed to analyse disruptions in epidemic dynamics at population scales, considering spatial and temporal variations, phenotypic plasticity, reproductive variability, and genetic factors. The team's statistical knowledge was instrumental in addressing several methodological and inferential challenges encountered in this thesis.

Thus, by combining these specialized competencies—ranging from computational modelling and deep learning to advanced statistical inference—this thesis tries to establish a robust interdisciplinary foundation, enabling innovative approaches to infectious disease diagnostics and management in livestock agriculture.

A multi-modal dataset for studying BRD in beef cattle farms

During this thesis, an extensive observational dataset was collected as part of the Septime Project (Carnot France Futur Élevage), a collaborative initiative involving the BIOEPAR research unit (INRAE) and Idele (the French Livestock Institute). The objective of project SEPTIME is to integrate real-time sensor data with mechanistic epidemiological models, enabling theoretical disease progression scenarios to be continually updated and adjusted according to observed field conditions.

Data acquisition (Fig 1.5) spanned two distinct periods aligned with the typical arrival schedules of cattle batches on farms: initially from January to June 2023, and subsequently from October 2023 to January 2024. These timeframes were specifically chosen based on evidence indicating that animals are at significantly elevated risk for Bovine Respiratory Disease (BRD) during the first few weeks following their arrival at new farms [180]. Accordingly, sensor recordings and veterinary assessments commenced immediately upon the animals' arrival and continued consistently over the subsequent 30 days—a period recognized as crucial for early detection and effective management of BRD.

This dataset was specifically designed to facilitate detailed studies of Bovine Respiratory Disease (that is why it was done in collaboration with veterinarians working on the scientific question to determine immunologic markers of BRD) and comprised observations from nine beef fattening farms located across France. Within each farm, data was collected from up to three separate batches of

cattle, each batch consisting of 5 to 12 animals. Approximately 78% of these animals were of the Charolais breed, specifically chosen for its distinctive white fur that allows clearer visual detection of clinical symptoms.

To ensure comprehensive monitoring, multiple sensor modalities were installed and utilized systematically across these farms. Specifically, each farm was equipped with, One fixed video camera recording daily segments of 5 minutes every hour between 9 a.m. and 6 p.m., one microphone synchronized with video recordings to capture acoustic data concurrently and one environmental sensor continuously measuring ambient temperature, humidity, carbon dioxide (CO_2), and ammonia (NH_3) levels. Veterinary oversight played a pivotal role in enriching the dataset, with regular professional assessments conducted approximately every two days throughout the 30-day observation period following batch arrivals. Assessments could involve both clinical and biological examinations: clinical examinations included evaluations of animal behaviour and observable clinical signs, such as fatigue, ocular discharge, nasal discharge, and rectal temperature. Biological examinations entailed laboratory analyses of blood samples and polymerase chain reaction (PCR) testing of nasal swabs to detect the presence of pathogens within the animals' upper respiratory tract.

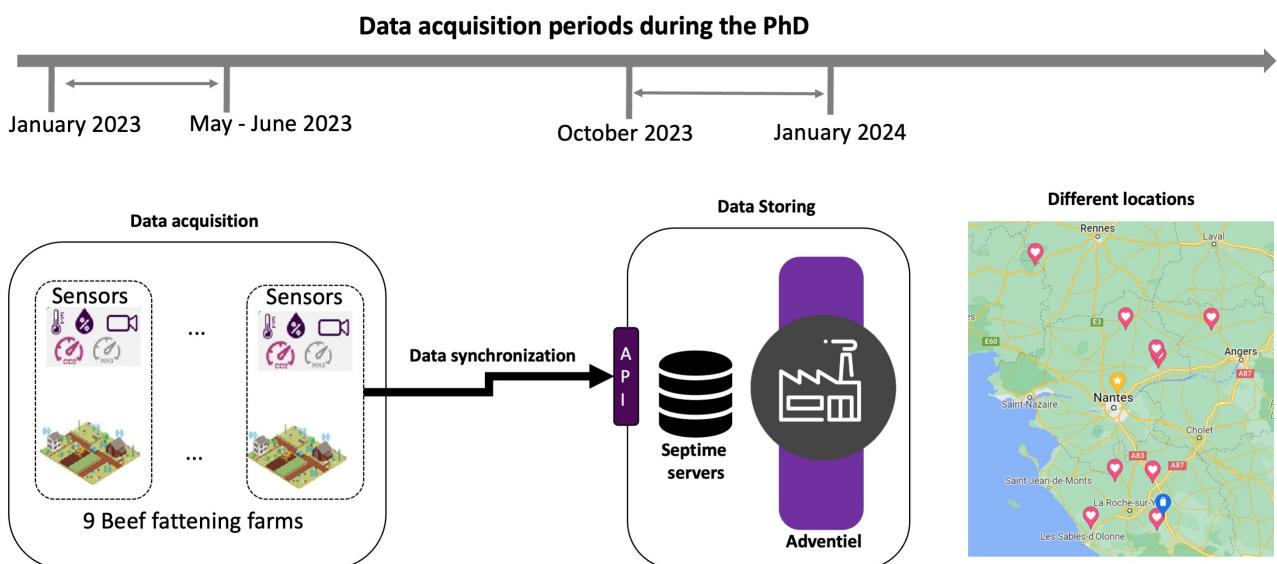


Figure 1.5: Overview of data acquisition protocol put in place for bovine respiratory disease monitoring

Additionally, lung ultrasound scans were periodically conducted as a complementary diagnostic method. These ultrasound examinations occurred on scheduled days (day 0, day 5, day 14, day 21, and day 28), depending on veterinarian availability. Ultrasound recordings provided detailed visual assessments of lung condition, enhancing the dataset's diagnostic depth. In parallel with the on-farm data collection, considerable effort was devoted to configuring reliable communication and secure data transfer between installed sensors and Adventiel's remote data storage servers. This integration was ensured that collected sensor observations were systematically organized, stored, and made readily accessible for subsequent statistical and computational analyses.

Collectively, this dataset—comprising synchronized multimodal sensor recordings, veterinarian clinical and biological assessments, and ultrasound imaging, has provided a solid empirical foundation that simultaneously addresses fundamental research questions and practical agricultural objectives. In the next subsection, we clearly explain how we proceeded to tackle our scientific question, which sensor observation, which first questions and the potential contributions we bring through our work.

About the methodological approach and contributions

The central methodological ambition guiding this thesis is to demonstrate how coupling deep learning methods with mechanistic epidemiological modelling can effectively leverage sensor-derived observations to enhance animal health through the study and the control of infectious disease in livestock farming. This integrative approach seeks to address the inherent uncertainties and practical limitations associated with sensor technologies (particularly when observations are sparse, noisy and incomplete) by employing powerful data processing methods and robust interdisciplinary theoretical knowledge into a novel modelling approach. We chose to test and assess our modelling approach to study and control BRD, as it is currently ongoing and challenging problem to tackle that has lots negative impacts (antimicrobial usage, public health safety, animal welfare, farmer wellbeing, etc)

Our investigation unfolds methodologically across three interlinked chapters, each addressing a distinct yet complementary facet of the overarching scientific inquiry. The journey begins in Chapter 2, where we set foundational structures to independently examine the feasibility and robustness of both deep learning and mechanistic models in the specific context of Bovine Respiratory Disease (BRD). We ask: "To what extent can deep learning reliably automate short-term diagnosis using limited and context-specific sensor data, such as lung ultrasound videos?" Using a tailored CNN-RNN architecture, we demonstrate the feasibility of automated diagnosis from limited observational data, achieving approximately 72% diagnostic accuracy on lung ultrasound videos collected in real-world farm conditions. Concurrently, we explore the second fundamental question: "Can empirical veterinary observations reliably be used to parametrize a mechanistic epidemiological model to provide long-term BRD prognosis?" Here, we successfully parametrize a stochastic mechanistic model using veterinary assessments, highlighting its potential for reconstructing disease dynamics over longer time horizons despite inherent uncertainties in sparse observations. These findings collectively provide an empirical baseline for further integrated analyses and constitute original contributions through the creation of a unique, annotated dataset of lung ultrasound observations, critical for future research. Inspired by the "Mixture of Experts" (MoE) concept, our methodological approach explicitly acknowledges and leverages the distinct strengths of each modelling approach. We strategically delineate diagnostic tasks, which are handled by deep learning due to their robust semantic feature extraction capabilities, from prognostic tasks, which mechanistic epidemiological models perform effectively due to their capacity for long-term dynamic prediction grounded in theoretical epidemiological principles. This systematic division of expertise ensures that each methodological component is utilized in the domain where it is most effective. Additionally, the unique annotated lung ultrasound dataset we have collected and labelled could represent a contribution and an invaluable resource for future research.

Building upon this foundation, Chapter 3 delves deeper into methodological complexities by explicitly addressing scenarios involving multiple plausible pathogen-specific mechanistic models. The central inquiry of this chapter is twofold: first, "To what extent can we reliably differentiate between multiple pathogen-specific mechanistic models of BRD solely based on symptomatic observations?", and second, "Does the identification of the correct pathogen-specific model significantly improve practical decision-making outcomes?". The necessity for multiple, specialized prognostic experts can be illustrated through a familiar medical analogy: when a patient experiences symptoms, they first consult a general physician who must then determine which specialist—whether a cardiologist, neurologist, or pulmonologist—should handle the diagnosis and subsequent treatment. Similarly, accurate long-term prognosis of BRD requires identifying the correct pathogen-specific mechanistic model (or "specialist") based on observed diagnosis to ensure that the resulting recommendations align effectively with disease-specific management strategies. To tackle these critical questions, we propose a novel methodological approach employing Approximate Bayesian

Computation coupled with multinomial logistic regression, successfully distinguishing pathogen-specific models (BRSV, Mh, and Mb) with approximately 93% accuracy based solely on observed symptomatic trajectories. Crucially, we further integrate these pathogen-informed predictions into a detailed bio-economic framework, demonstrating tangible improvements in farm-level decision-making outcomes—including a remarkable 44% reduction in antimicrobial use and a modest but meaningful increase in profitability. These results underscore the importance of rigorously linking epidemiological modelling with actionable decision-making, highlighting practical implications that extend beyond academic curiosity.

The narrative culminates in Chapter 4, where the methodological integration becomes explicit and adaptive. This final chapter poses two pivotal questions: "Can automated short-term diagnostics derived from limited sensor observations effectively specify a mechanistic epidemiological model for robust long-term disease prognosis?" and critically, "How can intrinsic uncertainties inherent in noisy sensor-derived diagnostic data be explicitly quantified and incorporated into prognostic predictions?" To address these questions, we present an innovative Bayesian Deep Mechanistic (BDM) approach, a structured hybrid model that explicitly integrates deep learning-based diagnostic predictions from lung ultrasound (LUS) video data with a mechanistic epidemiological model. By employing Monte Carlo Dropout (MCD), we systematically quantify and manage uncertainties inherent in the noisy, limited sensor data—effectively enhancing diagnostic accuracy from an initial 39% error to a robust 27.2% relative root mean squared error (RRMSE). This explicit uncertainty quantification not only substantially improves the robustness and reliability of short-term automated diagnostics but critically also enhances long-term disease forecasts. The dual methodological strategies explored, uncertainty-based filtering and uncertainty-weighted inference, demonstrate how explicitly incorporating uncertainties into mechanistic models significantly closes the predictive accuracy gap between purely automated sensor-based forecasts and expert-driven prognostics, thus providing a robust and practical decision-support tool for livestock management.

General discussion - The final section synthesizes the findings across all chapters, critically evaluating the methodological approaches, their strengths and limitations, and the broader implications of the results. Recommendations for future research and applications are also discussed, highlighting the potential for scalability and interdisciplinary adaptation. Across these chapters, the contributions of this thesis converge into a comprehensive methodological framework characterized by automated diagnostics, robust prognostics, clear model differentiation strategies, explicit uncertainty quantification, and practical decision-making integration. The modularity and flexibility of the approach developed here encourage its broader applicability across diverse epidemiological contexts, inviting domain experts, from veterinarians and deep learning specialists to mechanistic modellers, to further adapt and refine these methodologies.

1.4 [In french] Résumé grand public

La gestion des maladies infectieuses en élevage bovin s'inscrit dans un système d'une grande complexité, en raison de facteurs intrinsèques (par exemple la virulence des pathogènes et la sensibilité des animaux) et extrinsèques (pratiques d'élevage, conditions environnementales) en constante évolution. Face à cette complexité, l'intelligence artificielle (IA) émerge comme une approche prometteuse pour modéliser les dynamiques épidémiques et anticiper leur évolution via des simulations, fournissant ainsi des outils d'aide à la décision aux éleveurs, vétérinaires et autres acteurs. Parallèlement, l'essor de l'agriculture de précision se traduit par le déploiement de capteurs capables de surveiller en continu des variables physiologiques individuelles et des conditions environnementales, et de générer des alertes rapides (en quelques heures ou jours) sur des événements critiques

tels que le vêlage, les chaleurs, le bien-être ou la santé des animaux.

Néanmoins, s’agissant des maladies infectieuses en élevage, ces alertes issues de capteurs souffrent d’une faible spécificité et génèrent un taux élevé de faux positifs. Ces fausses alarmes imposent une charge mentale importante aux éleveurs, qui finissent soit par les ignorer faute de pertinence, soit par réaliser des interventions inutiles et coûteuses. Ainsi, concevoir des méthodologies innovantes capables de transformer ces signaux peu spécifiques en recommandations précises et actionnables sur des horizons de temps plus longs (plusieurs jours à plusieurs semaines) reste un défi de recherche ouvert. C’est précisément ce défi que cette thèse entreprend de relever, en posant la question centrale: comment exploiter efficacement les observations issues de capteurs pour étudier les maladies infectieuses et appuyer des décisions éclairées en élevage bovin ?

Pour y répondre, cette thèse postule qu’il est optimal d’intégrer des approches d’IA complémentaires, en l’occurrence les réseaux de neurones profonds et les modèles épidémiologiques mécanistes. La stratégie proposée capitalise d’une part sur la capacité des modèles mécanistes à représenter explicitement les processus épidémiques aux différentes échelles de temps en mobilisant les connaissances vétérinaires et biologiques, et d’autre part sur la puissance du deep learning pour extraire automatiquement des descripteurs pertinents à partir de données massives et hétérogènes issues des capteurs (images, sons, etc.). Le couplage de ces deux approches doit permettre une meilleure intégration des observations réelles (issues des capteurs, mais aussi des retours d’éleveurs et de vétérinaires) dans les prédictions épidémiques à court terme comme à moyen et long terme.

La problématique choisie pour appliquer cette méthodologie est celle des maladies respiratoires bovines (en anglais *Bovine Respiratory Disease*, BRD) chez les jeunes bovins de boucherie. La BRD constitue en effet le principal problème de santé dans les ateliers d’engraissement, avec des conséquences sanitaires et économiques majeures. Elle ralentit la croissance et la productivité des animaux, induit des frais vétérinaires et médicamenteux importants, et provoque une mortalité non négligeable (environ 3% en moyenne). C’est également la première cause d’usage d’antibiotiques en élevage bovin, avec près de 20% des bovins à l’engraissement recevant un traitement contre la BRD.

L’étiologie de la BRD est multifactorielle, résultant d’interactions complexes entre de nombreux facteurs. Côté animal, la susceptibilité dépend de la race, de l’état immunitaire et de la co-infection par divers agents pathogènes (notamment les bactéries **Mannheimia haemolytica** et **Pasteurella multocida**, ou des virus comme le virus respiratoire syncytial bovin), dont les interactions restent encore mal élucidées. Côté élevage et environnement, des facteurs de risque tels que le stress du transport, la densité des animaux, la gestion de l’alimentation, les conditions de logement, les protocoles de biosécurité ou le climat influencent fortement l’apparition et la gravité de la maladie. La conjonction de ces facteurs rend la prédiction et le contrôle de la BRD particulièrement hasardeux sur le terrain et complique sa modélisation épidémiologique.

En outre, la détection précoce de la BRD s’avère particulièrement ardue. Ses manifestations cliniques initiales — toux, écoulement nasal, fièvre, anorexie, léthargie, retard de croissance — sont peu spécifiques et peuvent facilement passer inaperçues, d’autant que les bovins ont tendance à dissimuler les signes de maladie aux premiers stades (comportement de proie). Les méthodes traditionnelles de surveillance visuelle présentent ainsi une sensibilité et une spécificité limitées (de l’ordre de 60 à 65% seulement), ce qui conduit à de fréquentes erreurs de diagnostic: des cas infectés peuvent ne pas être détectés à temps (faux négatifs), et inversement des animaux sains sont parfois traités à tort (faux positifs). Ces difficultés sont exacerbées par la pénurie de vétérinaires en zones rurales, qui restreint la possibilité d’une surveillance rapprochée et régulière des troupeaux.

La détection de la BRD pourrait néanmoins bénéficier des avancées récentes en élevage de précision, grâce au suivi continu de la santé des animaux par divers capteurs. Des accéléromètres, microphones, thermomètres connectés ou caméras permettent de mesurer des signaux physiologiques

et comportementaux associés à la maladie, tels que la température corporelle, les patterns d'activité ou les sons respiratoires. Par exemple, environ 73% des épisodes de fièvre (hyperthermie) chez des veaux à l'engraissement coïncident avec une BRD, ce qui suggère qu'une surveillance de la température peut être un indicateur utile. Plus récemment, un modèle statistique (régression logistique) exploitant des données de collier d'activité, de podomètre et de bolus intra-ruminal a atteint environ 75% de sensibilité et 76% de spécificité pour prédire l'apparition de signes cliniques de BRD jusqu'à 24 heures à l'avance. De même, des capteurs accélérométriques fixés sur les oreilles ont permis de détecter des changements de comportement (activité, rumination) distinguant clairement des veaux malades et sains, illustrant le potentiel des capteurs pour une détection plus précoce des maladies respiratoires bovines.

Pourtant, ces approches purement basées sur les capteurs demeurent limitées par l'utilisation de modèles d'apprentissage automatique traditionnels, peu aptes à extrapoler au-delà des situations déjà observées. Leur capacité à prévoir l'évolution d'une épidémie dans des contextes différents ou sur le long terme est réduite, ce qui limite leur utilité pour orienter les décisions de gestion sanitaire à moyen ou long échéance. Par ailleurs, il est éthiquement et pratiquement impossible de rassembler des données exhaustives couvrant tous les scénarios de BRD (en particulier les cas sévères) dans les conditions réelles d'élevage, ce qui freine inévitablement les méthodes purement empiriques.

En complément des capteurs, la modélisation épidémiologique mécaniste apporte une solution prometteuse pour dépasser ces limites observationnelles. Par exemple, une étude **in silico** récente a identifié des stratégies optimales de gestion de la BRD fondées sur des alertes capteurs. Cependant, les modèles mécanistes employés étaient calibrés à partir de données de la littérature vétérinaire plutôt que de données empiriques issues du terrain, introduisant des incertitudes quant à leur validité pratique. De plus, certaines solutions actuelles de détection reposent sur des dispositifs invasifs ou coûteux, d'où l'importance d'explorer des alternatives non invasives et abordables (analyse automatique d'images, d'enregistrements audio, etc.) pour une adoption à large échelle.

La stratégie de la thèse s'inscrit dans cette perspective et mise sur une forte interdisciplinarité en couplant apprentissage profond et modélisation mécaniste pour améliorer la détection et la prédition de la BRD. Ce travail a été mené dans le cadre d'une convention CIFRE, en partenariat étroit entre la société Adventiel et l'organisme de recherche INRAE, ce qui a favorisé le lien entre recherche académique et application industrielle. Adventiel, entreprise française spécialisée dans les solutions numériques pour l'agriculture, a apporté son expertise en intelligence artificielle appliquée (vision par ordinateur, analyse de signaux) ainsi que son infrastructure technologique (serveurs de calcul, stockage de données) pour la collecte et le traitement des observations issues des capteurs.

Du côté de l'INRAE, l'unité de recherche BIOEPAR (équipe DYNAMO) a fourni le cadre de modélisation mécaniste avec l'outil EMULSION — une plateforme à base de systèmes multi-agents et d'un langage dédié facilitant le développement de modèles épidémiologiques — et a partagé un premier modèle mécaniste de la BRD servant de base à cette étude. L'expertise vétérinaire et épidémiologique de BIOEPAR sur la BRD (connaissances cliniques, immunologiques et socio-économiques) a largement orienté la conception du modèle et l'interprétation des données. En parallèle, l'équipe Démécologie (unité IGEPP, INRAE) a contribué des méthodes statistiques avancées pour l'estimation des paramètres, la quantification des incertitudes et l'inférence bayésienne, afin d'aborder les défis liés à l'ajustement des modèles sur les données réelles. La synergie de ces compétences variées — modélisation, deep learning, statistique, expertise vétérinaire de terrain — confère à cette recherche un caractère original et illustre la convergence de multiples expertises autour d'un même objectif.

D'un point de vue empirique, une composante importante de la thèse a été la constitution d'un jeu de données multimodal inédit sur la BRD en conditions d'élevage réel. Cette collecte a eu lieu dans le cadre du projet collaboratif SEPTIME (Carnot «France Futur Élevage»), impliquant l'INRAE

(BIOEPAR) et l’Institut de l’Élevage (Idele). Elle s’est déroulée sur neuf exploitations d’engraissement bovin réparties dans différentes régions, lors de deux campagnes correspondant aux arrivées typiques de jeunes bovins: de janvier à juin 2023, puis d’octobre 2023 à janvier 2024. Ces périodes ont été choisies car les premières semaines suivant l’introduction d’animaux dans un nouveau troupeau sont connues pour présenter un risque élevé de BRD. Sur chaque élevage, un à trois lots de 5 à 12 bovins ont été suivis pendant 30 jours dès leur arrivée. Environ 78% des animaux étaient de race Charolaise, ce choix facilitant l’observation visuelle de certains symptômes grâce à la robe claire de ces bovins.

Le protocole de suivi mis en place combinait plusieurs capteurs et des examens vétérinaires réguliers. Chaque ferme était équipée d’une caméra vidéo fixe enregistrant un extrait de 5 minutes chaque heure en journée (de 9h à 18sh), d’un microphone synchronisé capturant les sons en parallèle de la vidéo (notamment la toux) et d’un capteur environnemental mesurant en continu la température ambiante, l’humidité, le CO_2 et l’ammoniac (NH_3). Parallèlement, les animaux ont été examinés par un vétérinaire environ tous les deux jours durant le mois suivant leur arrivée. Lors de ces visites, un examen clinique était réalisé (observation du comportement, détection de signes respiratoires tels que fatigue, écoulements oculaires ou nasaux, prise de la température rectale) et des prélèvements biologiques étaient effectués: analyses sanguines et écouvillonnages nasaux pour détecter les pathogènes respiratoires par PCR. En complément, des échographies pulmonaires ont été pratiquées à des jours prédéfinis (le jour de l’arrivée, puis les jours 5, 14, 21 et 28) afin d’évaluer visuellement l’état des poumons et de confirmer d’éventuelles lésions. L’ensemble des données collectées (vidéos, audio, mesures environnementales, observations cliniques, résultats de laboratoire et imagerie médicale) a été automatiquement transmis et stocké de façon sécurisée sur les serveurs d’Adventiel, constituant une base empirique riche et synchronisée pour les analyses ultérieures. Ce jeu de données unique, alliant signaux de capteurs et diagnostics vétérinaires détaillés, fournit un fondement solide pour répondre aux questions scientifiques tout en restant ancré dans les besoins concrets de l’élevage.

La démarche méthodologique de la thèse se décline en trois étapes complémentaires, correspondant aux chapitres principaux, afin d’apporter successivement des éléments de réponse à la question posée. (1) Tout d’abord (Chapitre 2), chaque approche a été évaluée séparément pour en établir la faisabilité et les limites propres. D’un côté, nous explorons dans quelle mesure un modèle d’apprentissage profond peut automatiser le diagnostic de la BRD à court terme à partir de données de capteurs limitées et spécifiques (en particulier l’analyse de vidéos d’échographie pulmonaire). De l’autre, nous examinons si des observations vétérinaires de terrain peuvent servir à paramétriser un modèle épidémiologique mécaniste afin de fournir un pronostic de la maladie sur le long terme. Les résultats obtenus confirment l’intérêt de chaque approche. Un réseau de neurones profond entraîné sur les séquences d’échographies pulmonaires parvient à détecter des lésions de BRD avec environ 72% de précision, malgré les conditions d’acquisition variées sur le terrain. Parallèlement, un modèle épidémiologique mécaniste calibré à partir des observations cliniques réussit à reproduire les tendances de l’infection sur plusieurs semaines, et ce malgré le caractère parcellaire des données disponibles. Ce double constat fournit un socle empirique pour l’analyse intégrée et s’accompagne de contributions notables, telle que la constitution d’un jeu de données original d’échographies pulmonaires annotées pour la BRD – un atout précieux pour de futurs travaux en diagnostic vétérinaire assisté par IA. Il met en lumière la complémentarité des approches: les tâches de diagnostic instantané sont confiées au deep learning, excellent pour extraire des caractéristiques complexes d’images ou de sons, tandis que le pronostic à long terme est dévolu au modèle mécaniste, qui s’appuie sur les bases théoriques épidémiologiques pour simuler l’évolution de la maladie dans le temps.

(2) La deuxième étape (Chapitre 3) aborde la variabilité des agents pathogènes pouvant être en cause dans la BRD et l’impact de cette variabilité sur le pronostic. Plusieurs modèles mécanistes

spécifiques peuvent en effet être envisagés selon le pathogène prédominant (par exemple un modèle calibré pour le virus BRSV, et d'autres pour les bactéries **M. haemolytica** ou **P. multocida**). Il devient alors crucial de déterminer, à partir des seuls symptômes observés, quel agent prédomine afin de choisir le modèle de prévision adéquat, et de vérifier si cette identification améliore les décisions sanitaires. Par analogie, tout comme un médecin généraliste oriente un patient vers un spécialiste approprié en fonction de ses symptômes, notre système doit pouvoir sélectionner le «modèle spécialiste» (viral ou bactérien) correspondant à la situation réelle afin d'affiner ses prédictions.

Pour ce faire, nous avons mis en œuvre une approche bayésienne originale combinant une méthode d'inférence par ABC (**Approximate Bayesian Computation**) et une régression logistique multinomiale. Cette méthode permet de différencier avec environ 93% d'exactitude entre plusieurs scénarios simulés de BRD, en identifiant lequel des pathogènes principaux (virus BRSV, **M. haemolytica**, **M. bovis**, etc.) correspond le mieux à la trajectoire de symptômes observée. Surtout, le fait d'intégrer la reconnaissance de l'agent causal dans le modèle conduit à des recommandations de gestion plus efficaces. À l'aide d'un modèle bio-économique simulant le fonctionnement de l'élevage, nous montrons qu'en adaptant les interventions au pathogène identifié, il est possible de réduire d'environ 44% le recours aux traitements antibiotiques, tout en améliorant légèrement la performance économique de l'atelier d'engraissement. Ce résultat illustre concrètement l'intérêt de lier étroitement la modélisation épidémiologique aux décisions de terrain: un pronostic mieux ciblé permet des actions plus pertinentes, bénéfiques à la fois pour la santé des animaux (moins de traitements inutiles) et pour la rentabilité de l'élevage.

(3) La troisième et dernière étape (Chapitre 4) réalise l'intégration effective des deux approches (diagnostic automatique et modélisation mécaniste) dans un cadre uniifié, tout en gérant explicitement les incertitudes inhérentes aux données de capteurs. L'enjeu est double : utiliser les diagnostics automatisés à court terme issus des capteurs pour informer le modèle mécaniste en vue d'un pronostic à long terme, et tenir compte de l'incertitude de ces diagnostics pour garantir la fiabilité des prévisions. Pour cela, nous avons développé une approche hybride nommée **Bayesian Deep Mechanistic** (BDM), qui intègre les prédictions d'un modèle de deep learning (appliquée notamment aux vidéos d'échographie pulmonaire) au sein d'un modèle épidémiologique de manière probabiliste. Concrètement, chaque préiction de l'IA est associée à un degré de confiance, estimé par la technique du **Monte Carlo dropout** afin de quantifier l'incertitude du réseau de neurones. Ces diagnostics «probabilisés» alimentent ensuite le modèle mécaniste de deux manières: soit en filtrant ou pondérant les observations en fonction de leur niveau d'incertitude (de façon à ne conserver que les informations jugées fiables), soit en intégrant directement cette incertitude dans l'inférence des paramètres du modèle. Un tel dispositif améliore nettement la précision et la robustesse du système global. Par exemple, l'erreur de prévision à long terme est réduite d'environ un tiers (de 39% à 27% d'erreur quadratique moyenne relative) lorsque l'on tient compte de l'incertitude des données capteurs dans le modèle. Ainsi, le cadre BDM rapproche les performances d'un pronostic automatisé de celles d'un expert humain, en combinant les atouts du deep learning et des modèles mécanistes tout en atténuant leurs faiblesses respectives grâce à une gestion rigoureuse des incertitudes. Il en résulte un outil d'aide à la décision fiable, transparent et adaptable pour le suivi des maladies infectieuses en élevage.

En synthèse, les travaux menés dans cette thèse démontrent l'intérêt d'approches d'IA hybrides pour l'étude et le contrôle des maladies infectieuses en élevage, en particulier dans le contexte de l'élevage de précision. L'étude de cas sur la BRD illustre comment le croisement du deep learning et de la modélisation mécaniste permet de dépasser les limites actuelles des capteurs en santé animale : on passe de simples alertes ponctuelles et peu spécifiques à un système intégré de diagnostic automatisé, de pronostic robuste à long terme et d'aide à la décision, le tout étayé par une quantification explicite de l'incertitude. Les résultats obtenus se positionnent par rapport à la littérature actuelle en

apportant tout à la fois des avancées méthodologiques (intégration bayésienne innovante, différenciation de modèles en fonction des pathogènes) et des bénéfices concrets pour l'élevage (réduction de l'usage inutile d'antibiotiques, amélioration du bien-être animal et optimisation économique). Bien que développée sur la BRD, l'approche proposée revêt un caractère générique et pourrait être transposée à d'autres maladies infectieuses en élevage (voire en santé des plantes), dès lors que des données de capteurs sont disponibles pour alimenter les modèles. Ce travail, fruit d'une collaboration étroite entre acteurs académiques et industriels, ouvre ainsi de nouvelles perspectives pour des systèmes de santé prédictive en élevage, combinant intelligence artificielle et expertise métier afin d'aider les éleveurs et les vétérinaires à prendre des décisions éclairées.

Chapter 2

Foundational structures: diagnosis and prognosis experts

2.1 Introduction

2.1.1 Contextual background

Ultrasonography, a common diagnostic modality in both human and veterinary medicine, is particularly valued for its non-invasiveness, portability, and rapid assessment capabilities. Specifically, in veterinary medicine, thoracic ultrasonography (TUS) is extensively employed as a quick, accurate, and practical method for diagnosing lung lesions associated with respiratory diseases such as Bovine Respiratory Disease (BRD). It provides an immediate, real-time assessment of lung pathology without the limitations of other imaging techniques such as radiography or computed tomography, which involve high costs, radiation exposure, and require specialized facilities and sedation or anesthesia [194]. Pulmonary ultrasound videos provide a direct view of the lung tissue, making them highly relevant for assessing the severity of respiratory diseases like BRD. TUS can accurately identify critical pathological features associated with disease severity and prognosis, including consolidated lung tissue, lobar pneumonia, abscess formation, and pleural effusion. In feedlot cattle, Timsit et al. (2019) [195] demonstrated that the maximal depth and area of lung consolidation measured at the time of bronchopneumonia diagnosis using TUS were significantly associated with an increased risk of disease relapse and negatively impacted animal growth performance. [195] Interpreting ultrasound images poses challenges even for skilled experts due to inherent limitations of ultrasonography. Ultrasound images typically appear as noisy, black-and-white visuals that provide limited detail, capturing only two-dimensional representations of tissue shapes and echo patterns. The presence of artifacts such as comet tails or reverberations, as well as the subjective nature of differentiating between subtle variations in lung tissue echogenicity, further complicates the interpretation of lung ultrasounds. Additionally, lung lesions must reach the pleural surface to become visible ultrasonographically, limiting the detection of deeper pulmonary pathology. Despite these limitations, thoracic ultrasonography remains highly valuable due to its real-time diagnostic capability, portability, and practical utility in large-animal field settings, offering immediate insights into disease severity and prognosis when assessing BRD outbreaks on-farm.

A stochastic mechanistic model, developed by Picault et al. (2022) [192], was created to study BRD propagation and evaluate the impact of farming practices, including pen size, risk levels of cattle, and antimicrobial treatments (individual versus collective metaphylaxis). The motivation behind

this model was the need to explore Pareto-efficient BRD management practices in different farming conditions, specifically assessing the balance between disease control effectiveness and antimicrobial usage. Twelve scenarios, reflecting various fattening systems characterized by differences in pen size (small pens of 10 animals vs. large pens of 100 animals), risk levels (low, high, and high risk mitigated by preventive antimicrobial treatment), and treatment protocols (individual or collective metaphylaxis), were evaluated. Model parameters were calibrated using existing empirical data and relevant veterinary literature. Results demonstrated that BRD occurrence, severity, and mortality were predominantly influenced by risk level and pen size. Large pens and higher risk levels consistently resulted in increased severity and higher mortality rates. The model also emphasized the effectiveness of collective antimicrobial treatments during fattening periods, particularly in large pens with high-risk scenarios, by significantly reducing disease severity and mortality despite the associated increase in antimicrobial usage. Conversely, implementing measures to reduce risk at pen formation provided the best overall outcomes, effectively minimizing both antimicrobial usage and cumulative disease duration. However, this mechanistic model had previously been mostly calibrated from existing veterinary literature, leading to uncertainties regarding its practical and explanatory utility with real-world veterinary data and highlighting the importance of future validation with empirical datasets to enhance its practical applicability.

2.1.2 Originality and objective of this Work

diagnosis and prognosis expertise

The SEPTIME project has enabled the collection of empirical data addressing critical knowledge gaps in Bovine Respiratory Disease (BRD), providing diverse datasets captured at varying temporal frequencies. Lung ultrasound videos (LUS) were recorded and employed due to its rapid, non-invasive capability for diagnosing respiratory conditions. Lung ultrasound videos were recorded as part of the data collection phase of the project. Although the dataset assembled within this project is extensive, the analysis presented in this chapter utilizes only a subset due to the limited number of observations available. The labelled observations from these LUS videos represent a valuable foundation for evaluating and benchmarking various modelling methods. However, the primary challenge addressed in this work pertains to the limited quantity of observations available at the time of analysis, which constrains the ability to establish robust long-term prognostic insights.

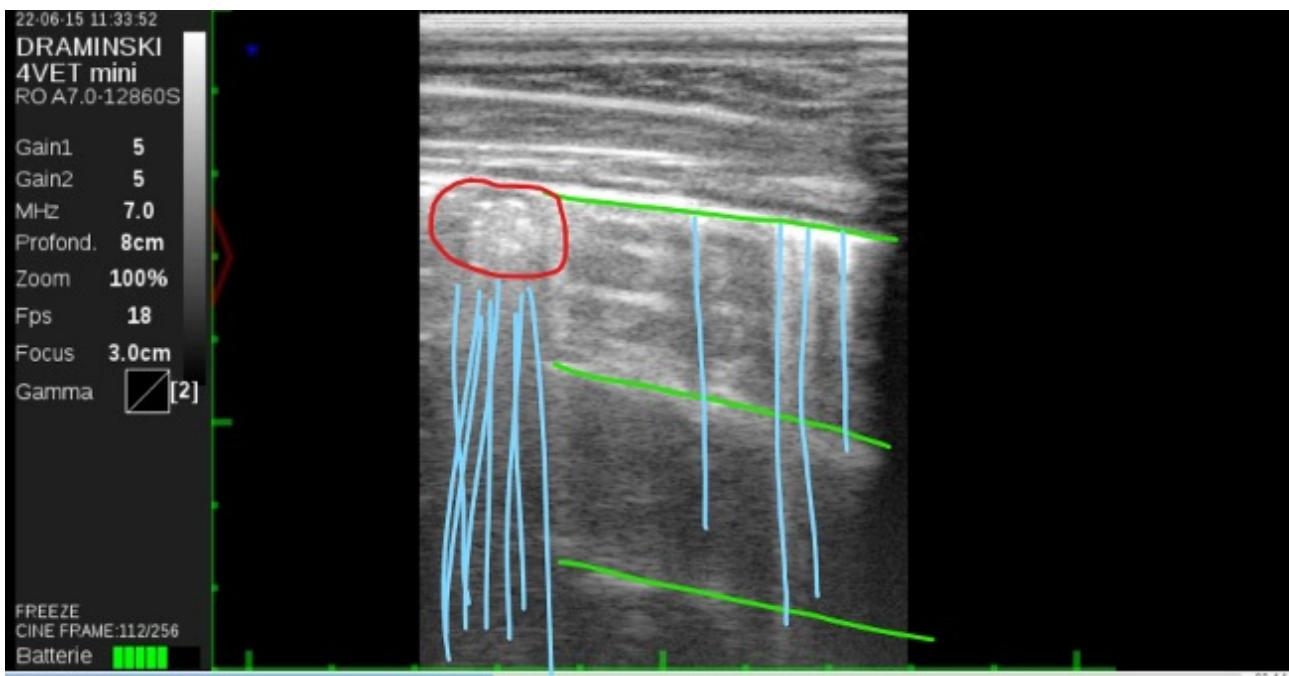


Figure 2.1: Pulmonary ultrasound

Achieving accurate and consistent results requires significant operator skill, training, and a systematic examination technique based on anatomical and ultrasonographic landmarks (fig 2.1). Variations in operator skill levels can result in differing degrees of diagnostic accuracy and reliability, making standardized training and experience crucial for correct implementation.

This study therefore addresses two scientifically complementary research questions, directly inspired by contextual gaps and illustrated by our methodological contributions:

To what extent can deep learning reliably automate short-term diagnosis using limited, and context-specific observational data from sensors, such as lung ultrasounds ? Unlike previous methods relying on manually extracted lesion characteristics [195], our objective is to evaluate the extent to which deep learning architectures can autonomously derive high-level semantic representations from lung ultrasound videos. We could then use this diagnosis expert to perform occasional diagnosis at different observation dates, this handles the need of a lot of data and could still provide first hand description of the health status (fig 2.2). We hypothesize that capturing the spatio-temporal patterns present in ultrasound videos through deep learning architectures can significantly enhance diagnostic robustness, particularly in field conditions where traditional manual lesion characterization is limited by subjectivity and variability. It might be lesion or it could another artefacts that the human eye wouldn't easily detect. This "sensor-to-diagnosis" automation could support veterinarians by offering immediate and objective assessments of animal health, providing valuable insight into the clinical state without extensive manual feature extraction or prolonged observational periods. Importantly, this approach could be practically deployed as a rapid and non-invasive technique to perform regular health monitoring, allowing veterinarians to obtain explicit, short-term descriptions of animal health status.

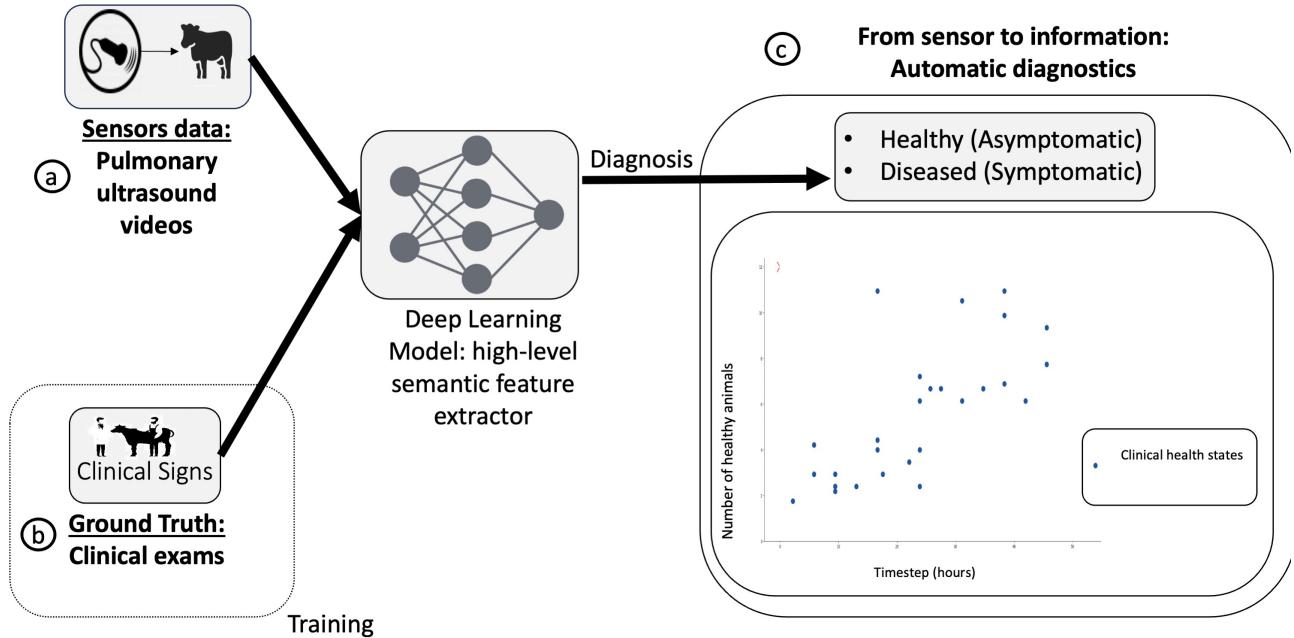


Figure 2.2: Can we use deep learning to automate the diagnosis at occasional date points using the limited available observations from sensors ?

Can mechanistic epidemiological models be parametrized using empirical veterinary observations to provide accurate explanatory long-term predictions for BRD ? The previously established stochastic mechanistic model for BRD propagation [192] was calibrated using theoretical assumptions rather than empirical veterinary observations, limiting its practical validation. In this work, we investigate whether empirical veterinary assessments considered ground truth, collected at limited temporal intervals and sparse frequency, can effectively parametrize a mechanistic epidemiological model to reliably predict BRD dynamics. Since daily health observations can be logistically challenging and costly in practice, we aim to assess whether accurate modelling can still be achieved by fitting the model to sparse empirical observations, allowing it to explicitly reconstruct disease dynamics and clinical states even on unobserved days (fig 2.3). Anything can happen in between the points, we could rely on the theoretical knowledge embedded in mechanistic models to explicit and give us evidence-based insights.

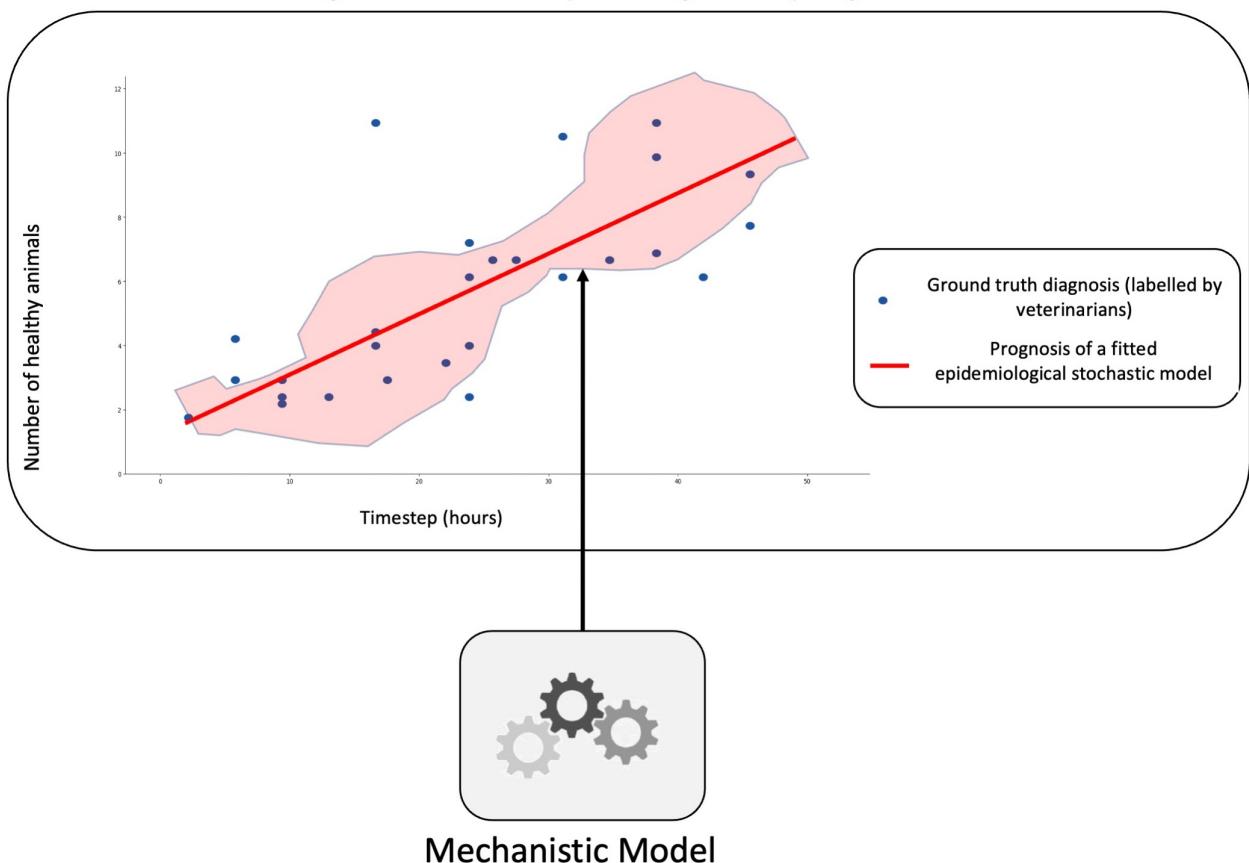
From diagnostic to in-depth long-term prognostic

Figure 2.3: Can a mechanistic model for BRD be fitted to real-world observations from veterinarians to predict at a larger temporal scale all the dynamics of BRD ?

2.1.3 Main contributions and perspectives

This research provided three core contributions:

1. Creation of an original dataset comprising pulmonary ultrasound videos with corresponding veterinary clinical annotations, providing a valuable resource for future BRD diagnostic and epidemiological research. Data collection occurred from January to June 2023, spanning a 30-day period post-arrival of calves on nine farms, each managing multiple batches of animals. Clinical annotations classified animals as symptomatic or asymptomatic according to veterinary-defined criteria (rectal temperature above 39.7°C and presence of at least one clinical symptoms such as cough or nasal discharge). Practical constraints, including animal immobilization, shaving the scan area, and veterinary availability, limited data quantity to approximately thirty annotated ultrasound videos.
2. Veterinary clinical assessments enabled the parametrization of the BRD mechanistic epidemiological model [192]. The sensitivity analysis conducted by Picault in 2022 revealed three parameters as the most influential in controlling BRD dynamics, antimicrobial usage, and mortality rates. These parameters are the **pathogen transmission rate**, which describes how rapidly an infectious agent spreads between animals; the **mean duration in the infectious state**, representing how long an infected animal can transmit the disease; and the **mean duration in the pre-infectious state**, indicating how long an animal remains exposed before becoming actively infectious. Accurate estimation of these parameters is critical because they substantially influence infection spread, disease severity, and effectiveness of control strategies, including antimicrobial use. This parametrization (fig 2.1) allowed predictions of BRD dynamics over a 30-day period, achieving forecasting accuracy with a root mean squared error (RMSE) below 5% in certain farms. However, the general applicability of the average pathogen model across all scenarios warrants caution. We hypothesize that this simplification could limit its accuracy in predicting outbreaks driven primarily by viral infections. Indeed, Picault himself stated, "our assumption that the same 'average' pathogen could be used for all scenarios is indeed questionable. BRD is intrinsically a multi-pathogen disease, and the exact prevalence of each pathogen, their possible interactions, as well as the diversity of strains, can be expected to change the dynamics of infection and disease severity [196, 197]. In this study we assumed an average pathogen to keep the model as simple as possible. However, in further study, model parameters reflecting microbiological characteristics (e.g., the mean duration of infectiousness and the pathogen transmission rate) could be made pathogen-specific to allow for comparisons between various pathogens."

Parameter name	Farm 1			Farm 2			Nominal values Calibrated
	Median	Q1	Q3	Median	Q1	Q3	
Pathogen Transmission 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

Table 2.1: Inferred values of parameters vs nominal value of parameters

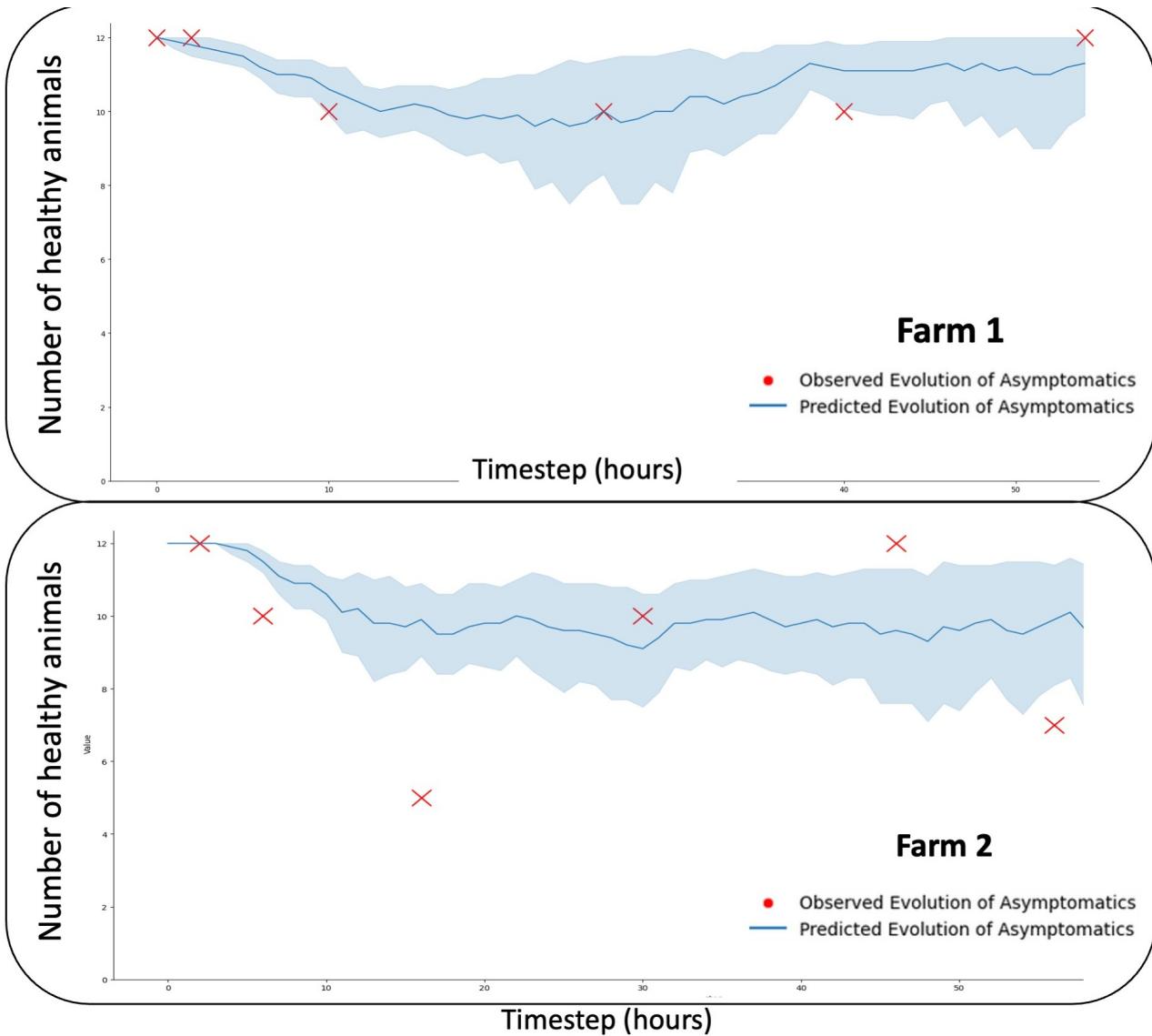


Figure 2.4: Asymptomatic forecast: ground truth vs predictions of an average pathogen mechanistic model

3. A deep learning model based on a spatio-temporal CNN-RNN architecture was trained to classify animals' clinical health status (symptomatic or asymptomatic) using pulmonary ultrasound videos. This model achieved an accuracy of approximately 72% (table 2.2). Specifically, the deep learning architecture combined convolutional neural networks (CNNs), serving as spatial feature extractors, and recurrent neural networks (RNN), which captured temporal information. Throughout the experiments, only the feature-extractor component—the CNN architecture—was varied, while the RNN architecture remained fixed across all tested models. The CNN's goal was to identify and extract relevant spatial features within individual ultrasound frames, such as lesions, pleura lines, or other anatomical details indicative of BRD. Conversely, the RNN aimed to leverage temporal sequences of these extracted features to model their evolution over the video duration. Different CNN architectures were evaluated, including EfficientNetB7, InceptionResnetV2, InceptionV3, VGG16, and an ensemble model combining InceptionV3 with InceptionResnetV2. Among these architectures, InceptionV3 achieved the highest performance, with a weighted F1-score of 70%, precision of 72%, recall of 69%, and an overall accuracy of 69%. In contrast, VGG16 demonstrated significantly lower performance, yielding an F1-score of only 14%. The performance of the final selected deep learning model was assessed on two separate farms to verify its robustness and generalizability under con-

trasting practical conditions.

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

Table 2.2: Diagnosis performance of different deep learning architecture

These results demonstrate the individual feasibility of both diagnostic automation using deep learning and epidemiological prognosis via mechanistic modelling. However, the two phases—diagnosis and prognosis—were not yet integrated into a complete predictive pipeline. Results highlighted the limitations of employing an average pathogen model universally, as BRD is intrinsically a multi-pathogen disease, and pathogen-specific variations significantly influence infection dynamics and disease severity. In the next chapter, methodologies for selecting the optimal prognosis expert model from multiple alternatives using outbreak observations will be discussed.

2.1.4 [In French] Résumé grand public

La maladie respiratoire bovine (BRD) est une pathologie fréquente et complexe qui représente un défi majeur en élevage, entraînant des pertes économiques importantes liées aux traitements, à la diminution des performances zootechniques et à une mortalité accrue. Afin de diagnostiquer cette maladie, les vétérinaires ont parfois recours à l'échographie pulmonaire, une méthode rapide, non invasive et réalisable directement à la ferme grâce à des appareils portables. Ces appareils, utilisés habituellement pour l'échographie reproductive chez les bovins, permettent d'examiner rapidement les poumons des animaux sans exposition à la radiation, contrairement à la radiographie ou au scanner. L'échographie pulmonaire peut identifier précisément et rapidement certaines lésions pulmonaires associées à la BRD, telles que la consolidation des lobes pulmonaires, les abcès ou encore les épanchements pleuraux. Ces lésions échographiques sont d'autant plus importantes qu'elles peuvent indiquer la gravité de la maladie, prédire les rechutes et renseigner sur les performances futures des animaux atteints.

Le projet SEPTIME, dans lequel s'inscrit ce travail de thèse, a permis la collecte de nombreuses données empiriques issues d'échographies pulmonaires enregistrées directement dans des élevages bovins durant les années 2023 et 2024. À partir de ces vidéos échographiques annotées par des vétérinaires experts, nous avons exploré deux approches complémentaires afin d'améliorer le diagnostic et le pronostic de la BRD :

1. L'utilisation de modèles d'intelligence artificielle (apprentissage profond) permettant d'automatiser rapidement la détection des cas cliniques de BRD à partir d'échographies pulmonaires. Ces modèles montrent un bon potentiel avec une précision atteignant environ 72% dans la reconnaissance automatique de la maladie.

2. Le paramétrage et l'évaluation d'un modèle mécaniste épidémiologique, qui simule la propagation à long terme de la maladie à partir d'observations réelles issues du terrain. Ce modèle mécaniste, une fois calibré, permet de prédire efficacement l'évolution de la maladie sur plusieurs semaines et pourrait ainsi aider les éleveurs à anticiper les épidémies et à adapter leurs stratégies de gestion sanitaire.

Ces résultats démontrent la faisabilité individuelle de l'automatisation du diagnostic et du pronostic à l'aide de l'apprentissage profond et du pronostic épidémiologique via la modélisation mécaniste. Le chapitre suivant aborde les méthodologies de sélection du modèle expert de pronostic parmi de multiples alternatives en utilisant des observations cliniques.

2.2 Proceedings published in Society for Veterinary Epidemiology and Preventive Medicine, 2024



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

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

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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

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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.

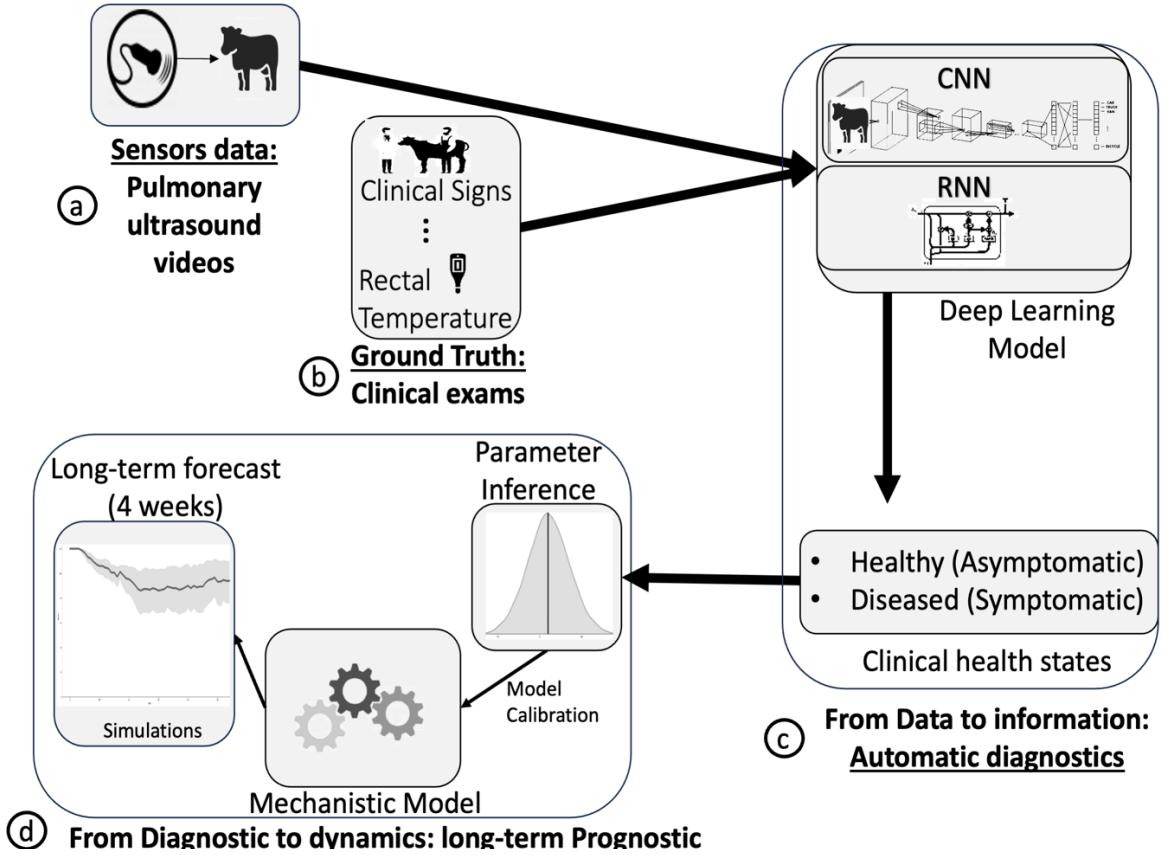


Figure 1. Workflow of the “deep mechanistic model” approach. This hybrid approach integrates a deep learning model (data-driven) with a mechanistic model (knowledge-driven)

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 cm² 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 imangenet, 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 employs 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).

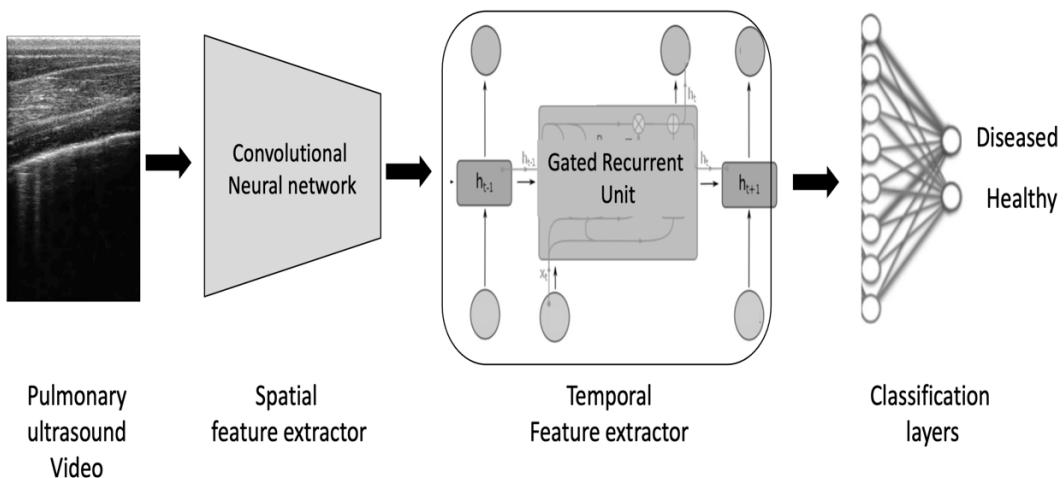


Figure 2. Deep learning Architecture Trained

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.

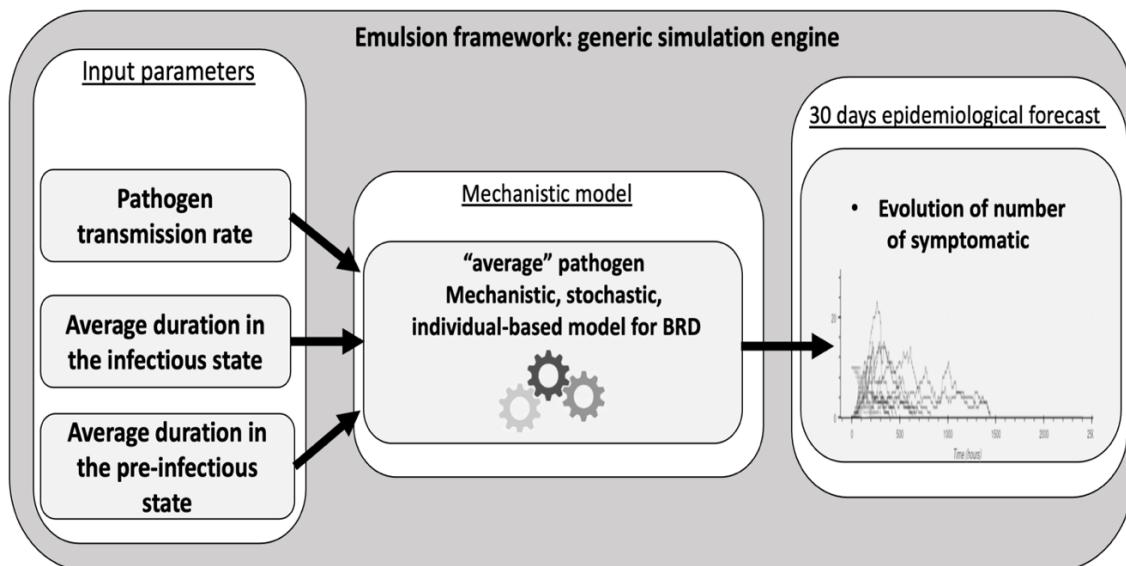


Figure 3. Simplified process of how the average pathogen model was used

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.

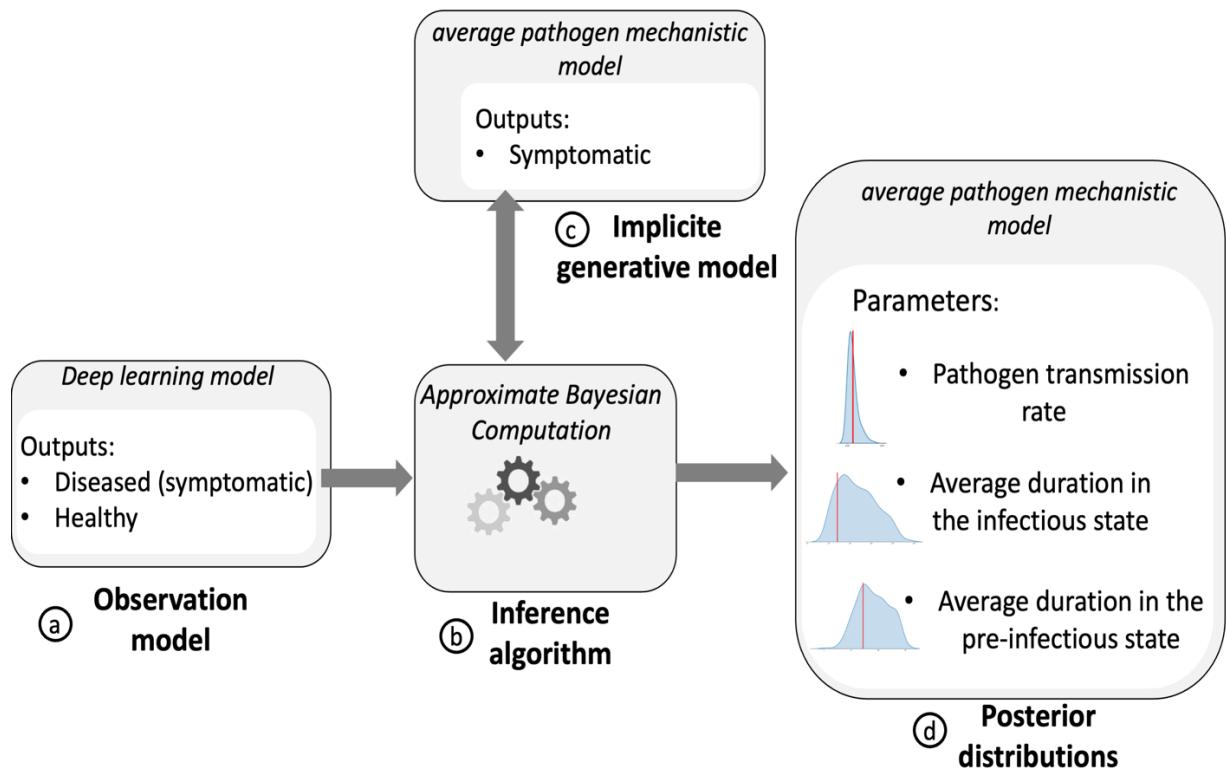


Figure 4. Method of coupling a deep learning model with a mechanistic model. Inference of the three biological parameters of an average pathogen BRD model

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 +	0.71	0.62	0.63	0.62
InceptionResnetV2				

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 ± 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%.

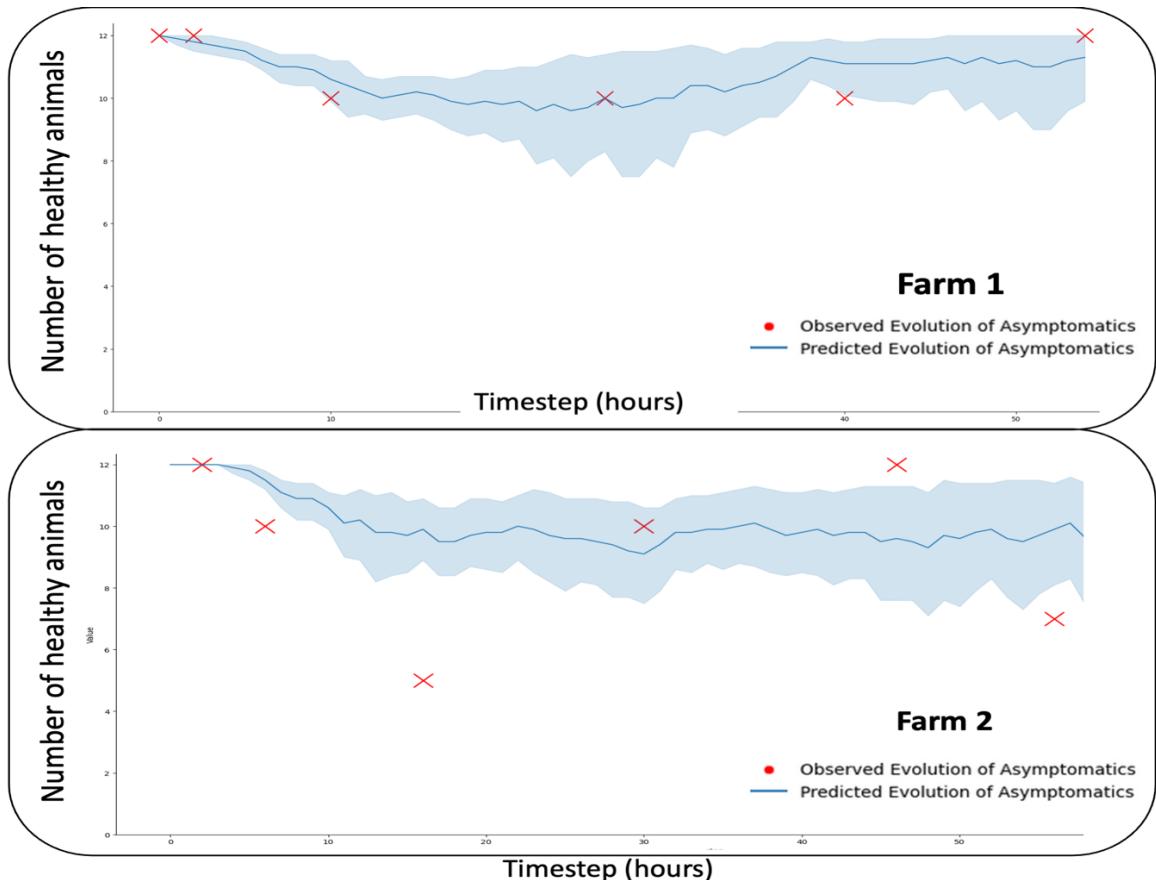


Figure 5. Asymptomatic forecast, ground truth vs calibrated average pathogen mechanistic model

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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Chapter 3

Structural synergism in bovine respiratory disease modelling

3.1 Introduction

3.1.1 Contextual background

Mathematical modelling has emerged as a cornerstone for evidence-based decision-making in animal health, increasingly recognized as indispensable by policy makers and veterinary epidemiologists [198, 199]. Modelling frameworks offer a structured approach to understanding disease dynamics, quantifying transmission risks, forecasting outbreaks, and evaluating intervention strategies. In veterinary epidemiology, and particularly in the management of complex multi-pathogen diseases like Bovine Respiratory Disease (BRD), mathematical models serve as powerful tools that integrate knowledge across multiple disciplines, including epidemiology, veterinary science, agricultural management, and economics.

BRD is inherently complex due to its multifactorial nature, characterized by interactions between various pathogens, host susceptibility, environmental stressors, and management practices. Numerous mechanistic epidemiological models have been proposed to capture this complexity [192, 200]. However, the mechanisms governing pathogen interactions, co-infections, and the clinical manifestations of BRD remain incompletely understood. Consequently, existing models often differ significantly in their structure, underlying assumptions, and levels of biological detail. These structural differences create uncertainties in predictions, complicating the practical task of identifying a model that accurately reflects real-world outbreak dynamics.

Recent developments emphasize the advantages of using pathogen-specific mechanistic models instead of generalized "average pathogen" approaches. Pathogens such as *Orthopneumovirus bovis* (formerly known as the Bovine Respiratory Syncytial Virus, in short BRSV), *Mannheimia haemolytica* (Mh), and *Mycoplasmopsis bovis* (formerly *Mycoplasma bovis*, Mb) exhibit distinct epidemiological characteristics, clinical progressions, and treatment responses, each requiring targeted intervention strategies. Recognizing this diversity, pathogen-specific models have been advocated for their enhanced realism and predictive accuracy in simulating BRD outbreaks. Beyond parameterization challenges, the comparative assessment of multiple valid mechanistic models necessitates addressing critical methodological dimensions. Model distinguishability, assesses whether competing models produce sufficiently distinct predictions, thereby enabling pathogen-model identification

from clinical observations. Secondly, and most practically relevant, is the concept of decision impact assessment, evaluating whether the selection of a given model actually translates into measurable, economically viable, and actionable improvements on the farm. These two interconnected methodological challenges underscore the need not only for rigorously validated mechanistic models but also for frameworks capable of linking theoretical model selection directly with improved decision-making outcomes.

3.1.2 Originality and objective of this work

This chapter focuses on two scientifically complementary research questions, driven by critical contextual and methodological challenges highlighted above:

To what extent can we reliably differentiate between multiple pathogen-specific mechanistic models of BRD, solely based on symptomatic observations ? In this chapter, we introduce a numerical approach aimed at distinguishing among competing BRD mechanistic epidemiological models [200] based exclusively on observed symptomatic trajectories. Specifically, we show a general theoretical framework for pathogen-model identification, a critical issue across epidemiological contexts where accurate differentiation between pathogens is challenged by symptom overlap. The relevance of this work extends beyond Bovine Respiratory Disease (BRD), offering a broadly applicable solution for any epidemiological scenario involving multiple plausible mechanistic hypotheses or co-existing pathogens that necessitate distinct pathogen-specific management strategies. *Orthopneumovirus bovis* (BRSV) model captures rapid, airborne viral transmission dynamics, characterized by acute and intense infection episodes. It explicitly incorporates compartments for partial immunity, primary infection, potential reinfection (with reduced infectiousness), and rapid progression from mild to severe clinical signs, making the outbreaks swift but relatively short-lived. *Mannheimia haemolytica* (Mh) is modelled as an opportunistic infection primarily triggered by host immunosuppression or environmental stressors. Unlike the BRSV model, the Mh model does not account for re-infection states but includes a clear transition from asymptomatic carriage to active infection states, which can escalate into severe clinical manifestations. The infection dynamics are less explosive compared to BRSV, emphasizing progression triggered by stress-induced susceptibility. The *Mycoplasmosis bovis* (Mb) model structurally mirrors the Mh model regarding compartments (asymptomatic carriers transitioning to symptomatic stages). However, it notably differs by emphasizing chronicity and persistence. This pathogen exhibits slower transmission, prolonged infection durations, and intermittent clinical symptom manifestation, making early detection and timely treatment more challenging and resulting in prolonged circulation within cattle populations. The probability that a treated animal recovers (for 1 dose) is set to 71% for Mh and 60% for Mb. The models were calibrated using from the literature: probabilities of recovery with antibiotic treatment (single dose) are set at 71% for Mh and 60% for Mb.

Does the distinction and identification of the most likely pathogen-specific mechanistic model significantly improve practical decision-making outcomes ? In typical cattle farming practices (conventional treatment decisions), antibiotic treatments for Bovine Respiratory Disease (BRD) are usually administered empirically based solely on observable clinical signs, without reliable pathogen identification. Under these conditions, farmers treat all symptomatic animals with antibiotics, regardless of whether the underlying infectious agent is bacterial or viral. Since antibiotics are effective only against bacteria and not viruses, this approach frequently leads to inappropriate use of antibiotics, which has two main drawbacks: if the infectious agent is viral, antibiotic treatments are unnecessary, ineffective, and economically wasteful. Such misuse increases antimicrobial

resistance risks without any animal health benefit. If the infectious agent is bacterial, antibiotics are warranted and beneficial; failure to correctly administer them could lead to severe economic losses and compromised animal welfare.

To address this issue, we explicitly incorporate an economic dimension into our analysis by integrating pathogen-specific model predictions into a bio-economic framework. This enables us to quantify practical benefits, such as reductions in antibiotic usage, improved animal health outcomes, and enhanced profitability directly resulting from pathogen-informed decisions. By explicitly evaluating these consequences, our work connects theoretical epidemiological modelling with tangible, farm-level decision-making, reinforcing the practical relevance of modelling for effective livestock management.

3.1.3 Main contributions and perspectives

prognostic expert identification via model distinguishability

Our primary methodological contribution involves numerically distinguishing three mechanistic BRD models tailored for Orthopneumovirus bovis (BRSV), Mannheimia haemolytica (Mh), and Mycoplasmopsis bovis (Mb) [200]. First, We constructed synthetic outbreak scenarios representative of French beef cattle farms. Three discrete-time, stochastic agent-based, pathogen-specific model were utilized to generate outbreak trajectories over 277 days, capturing symptomatic dynamics every 12 hours for a batch of 12 calves. Variations across scenarios reflected realistic risk compositions, yielding a dataset comprising 13,650 individual simulations. Secondly, Three pathogen-specific stochastic, compartmental models [200] were compared, each encapsulating different transmission dynamics. Given the stochastic complexity of models and intractable likelihood functions, we employed Approximate Bayesian Computation (ABC) combined with multinomial logistic regression to identify the most likely pathogen-specific model. The ABC approach quantitatively assessed model distinguishability using summary statistics (detected symptomatic trajectories), thus allowing informed selection of the pathogen responsible for observed outbreaks. Given the stochastic complexity of models and intractable likelihood functions, we employed Approximate Bayesian Computation (ABC) combined with multinomial logistic regression to identify the most likely pathogen-specific model. The ABC approach quantitatively assessed model distinguishability using summary statistics (detected symptomatic trajectories), thus allowing informed selection of the pathogen responsible for observed outbreaks. Using synthetic symptomatic data generated under realistic farm conditions, we successfully identify the most likely pathogen-specific model with an average accuracy of approximately 93% (fig 3.1). Key performance metrics (true positive rates: BRSV=96%, Mh=90%, Mb=87%) clearly indicate the feasibility and reliability of pathogen identification based on early symptomatic trajectories.

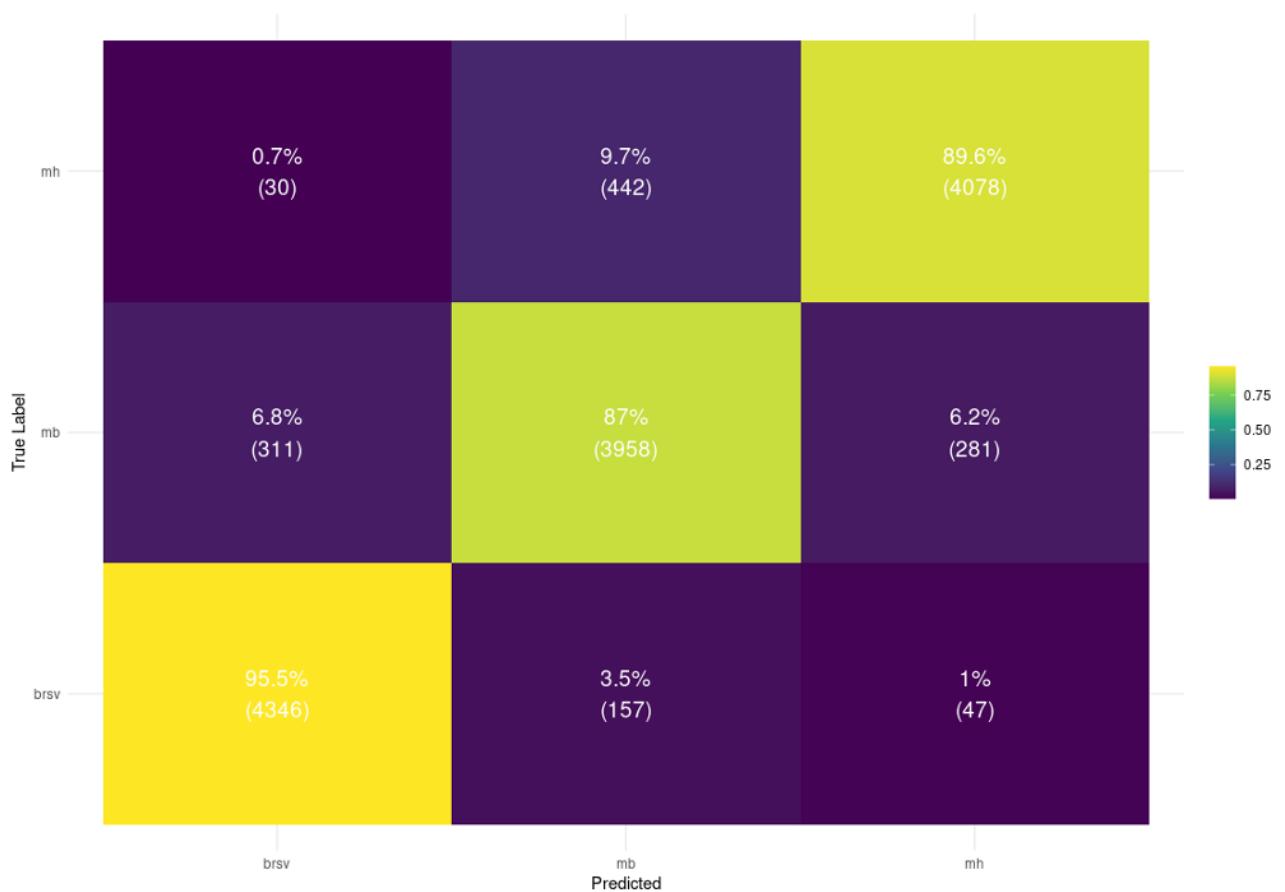


Figure 3.1: Confusion matrix. Classification performance for BRSV, Mh and Mb. The diagonal represents correctly classified instances, while off-diagonal values indicate misclassification between classes.

Decision-intelligence: measuring and improving the impact on decision-making

The second major contribution involves integrating pathogen-specific epidemiological models into a detailed economic evaluation framework. This integration enables us to quantitatively assess the economic impact of adopting pathogen-informed treatment decisions versus conventional empirical treatment strategies. Our economic model accounts explicitly for weight gain, carcass quality, feed, antibiotic treatment costs, and veterinarian interventions, calculating expected net profits and antibiotic usage for simulated cattle batches. We showed that pathogen-informed decisions substantially reduce antimicrobial use by approximately 44% (fig 3.2) in these conditions, directly addressing critical issues like antimicrobial resistance and public health safety. Simultaneously, these pathogen-informed strategies lead to a modest yet consistent increase (around 1%) in net profitability, highlighting that economic viability can be maintained or improved even when reducing antibiotic treatments.

By leveraging the high accuracy (93%) of pathogen-model distinguishability, we maximize the likelihood that the correct treatment decision, either antibiotic administration for bacterial infections or withholding antibiotics for viral infections—is consistently taken. This accuracy directly improves decision-making outcomes by: Increasing the frequency of correct recommendations, thus ensuring targeted treatments that align with actual disease aetiology. And reducing incorrect or harmful decisions (false positives and false negatives), significantly decreasing inappropriate antibiotic use and associated economic and public health costs.

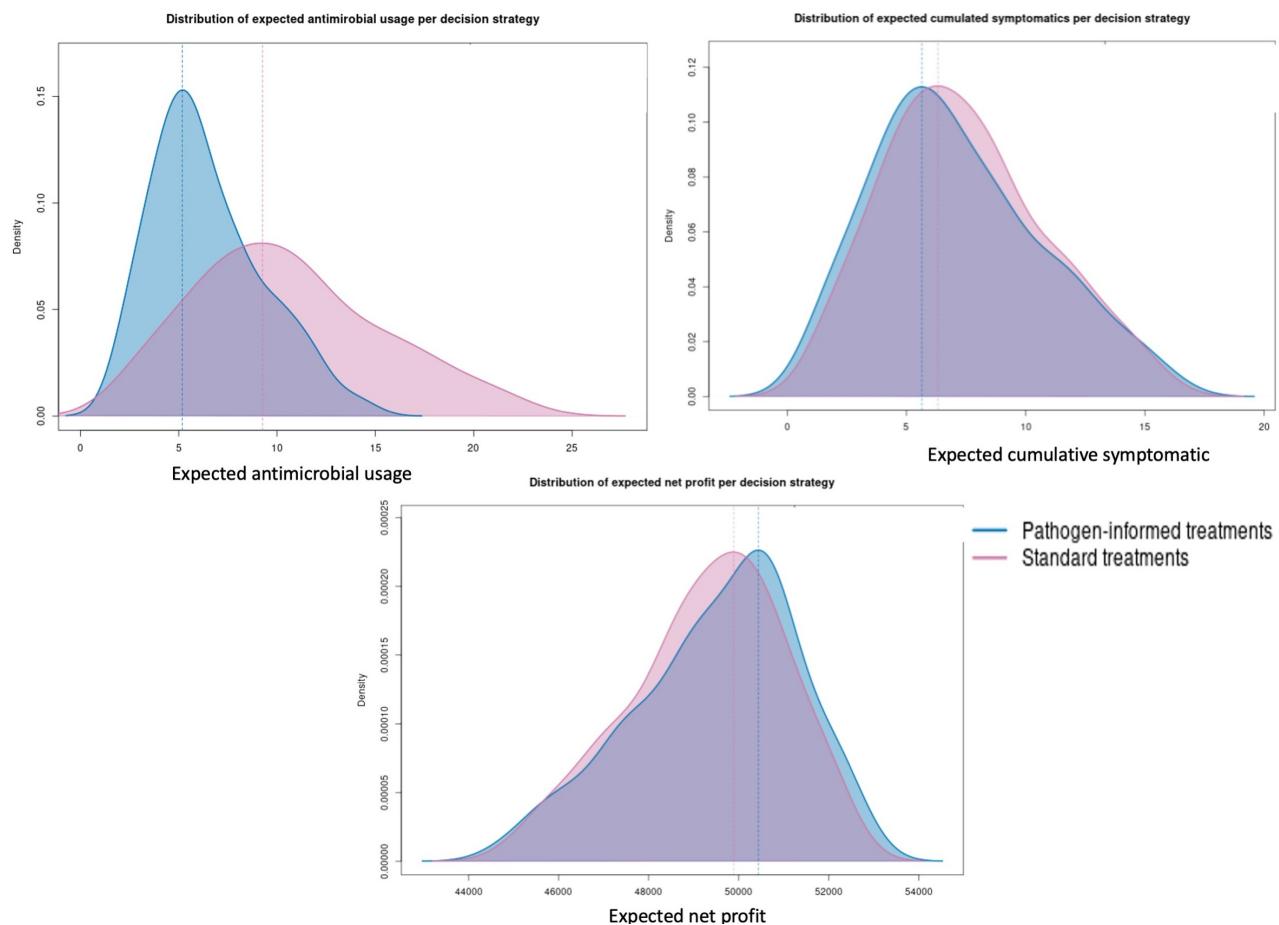


Figure 3.2: Pathogen informed treatment decisions versus conventional treatment decisions.

Perspectives

This work bridges theoretical epidemiological modelling with practical decision-making, emphasizing the importance of model distinguishability not only theoretically but as a practical tool for veterinary epidemiology and livestock management. Our approach is broadly applicable to scenarios where pathogen differentiation based solely on observations remains challenging yet essential. In the next chapter, we further explore integrating a real-world observation (sensor-based) for immediate diagnostic insights (deep learning-driven) with longer-term, prognosis-oriented mechanistic epidemiological models, combining these two forms of expertise to generate actionable disease management recommendations.

3.1.4 [In French] Résumé grand public

La gestion efficace des maladies respiratoires bovines (BRD) constitue un enjeu crucial pour la santé animale et pour l'économie des élevages bovins. Ces maladies sont complexes car elles impliquent souvent plusieurs pathogènes différents, notamment des virus comme Orthopneumovirus bovis (BRSV), et des bactéries telles que Mannheimia haemolytica (Mh) ou Mycoplasmosis bovis (Mb). Chaque pathogène possède ses propres particularités en matière de transmission, de symptômes et de réponse au traitement, rendant leur identification précise essentielle pour une gestion optimale.

Dans ce chapitre, nous avons proposé une approche basée sur la modélisation mécaniste afin d'identifier quel pathogène est à l'origine d'une épidémie, simplement à partir des symptômes ob-

servés chez les animaux. Notre méthode utilise des modèles mécanistes spécifiques à chaque pathogène, pour déterminer avec fiabilité l'agent responsable d'une épidémie sur une exploitation. Grâce à des simulations numériques réalistes, nous avons montré que cette identification est possible avec une précision élevée (environ 93% en moyenne).

Cette identification précise présente des avantages pratiques majeurs pour les éleveurs. Aujourd'hui, faute d'identification fiable, les traitements antibiotiques sont souvent administrés à tous les animaux symptomatiques sans distinction, même si certains souffrent d'infections virales pour lesquelles les antibiotiques sont inefficaces. Cette pratique entraîne une utilisation excessive et inutile des antibiotiques, augmentant le risque de résistance bactérienne, tout en générant des coûts économiques inutiles. Notre étude démontre que l'intégration de ces modèles spécifiques dans une démarche décisionnelle permet une réduction d'environ 44% de la consommation d'antibiotiques tout en maintenant, voire en augmentant légèrement (1%), la rentabilité des exploitations.

Ainsi, ce travail met en évidence l'intérêt concret des modèles mécanistes pour améliorer les décisions pratiques en élevage, réduisant à la fois les coûts économiques et les risques sanitaires liés à une mauvaise utilisation des traitements. Cette approche pourrait s'appliquer à d'autres contextes épidémiologiques où identifier précisément le pathogène à partir de simples observations cliniques reste un défi majeur.

3.2 Preprint in bioarxiv, 2025

1 Identifying bovine respiratory disease infectious agents via
2 mechanistic modelling and symptomatic dynamics: application for
3 optimal pathogen-informed treatment interventions

4

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15 **Abstract (max 250 words)**

16

17 Bovine Respiratory Disease poses significant health and economic challenges in the cattle industry.
18 Mechanistic modelling offers a powerful alternative to understand BRD transmission and evaluate
19 the efficiency of various control strategies. In this study, we investigate three pathogen-specific
20 models representing the Orthopneumovirus bovis(BRSV), *Mannheimia haemolytica* (*Mh*), and
21 *Mycoplasmopsis bovis* (*Mb*) to simulate outbreak trajectories. Given the intractability of these model's
22 likelihood functions, we employ approximate bayesian computation, a numerical approach to assess
23 model distinguishability and identifiability across diverse outbreak scenarios representing several
24 initial risk compositions. By selecting the model that best fits early symptomatic dynamics, we infer
25 the most likely causative infectious agent and make informed individual antibiotic administration
26 decisions. Furthermore, we integrate an economic model to assess expected benefits of different
27 antibiotic treatment strategies. Results demonstrate a strong early infectious agent identification
28 performance with an average accuracy of 93%. Findings also highlight that pathogen-informed
29 treatment decisions substantially and consistently decreases antimicrobial usage (44%) across batch
30 configurations, contributing against the emergence of antimicrobial resistance. Informed-decisions
31 strategies also led to an overall moderate increase in net profit of 1%. This work, paves the way for
32 developing user-centered decision-support tools for BRD control.

33

34 **Keywords:** BRD pathogen inference, non-local numerical model distinguishability,
35 decision-informed control measures, Bioeconomic impact of informed-decisions,
36 computational epidemiology, decision intelligence

39

40

1. Introduction

41 Bovine Respiratory Disease (BRD) is one of the most significant health and economic challenges
 42 in the cattle industry, representing a substantial burden globally (Babcock et al., 2009; Delabouglise
 43 et al., 2017). Its economic impact is profound, with costs estimated to reach 20% of farmers' income
 44 in France and up to 44% in North America (Bareille et al., 2009; Mijar et al., 2023). BRD is a highly
 45 infectious, multifactorial disease affecting both the upper and lower respiratory tracts. It is
 46 commonly caused by co-infections of viruses and bacteria and is often exacerbated by abiotic
 47 stressors such as transportation stress (Grissett et al., 2015; Kudirkiene et al., 2021). In Europe, the
 48 most frequently reported pathogens include bacterial agents such as *Mycoplasmopsis bovis* (Mb)
 49 and *Mannheimia haemolytica* (Mh), alongside viral agents like Orthopneumovirus bovis(BRSV)
 50 and Respirovirus bovis (PI3) (Grissett et al., 2015). Diagnosing BRD is challenging due to the
 51 interplay of multiple factors, such as the nature of pathogens, animal genetics, and farming
 52 management practices (Gaudino et al., 2022; Murray et al., 2017). There is no global common
 53 threshold to determine whether an animal is diseased from clinical signs (fever, nasal discharge...)
 54 because clinical signs are non-specific to BRD, making precise pathogen identification difficult
 55 (Wolferger et al., 2015). Moreover, visual detection often results in delayed diagnoses. For instance,
 56 there can be a lag of up to 51 hours between the onset of hyperthermia episodes caused by the
 57 disease and observable clinical signs (Timsit et al., 2011). Laboratory tests such as multiplex PCR,
 58 while more accurate, are costly (up to \$150 per sample) and time-consuming, taking days to yield
 59 results (Thonur et al., 2012). Due to these diagnostic challenges, usually during an outbreak,
 60 causative pathogens are not precisely identified by farmers (Griffin et al., 2014; Ollivet et al., 2020).
 61 Antibiotics remain the primary control measure (Ollivett et al., 2020; Brault et al., 2019; Nickell &
 62 White, 2010), with farmers relying on visual signs of severe illness for treatment decisions (Ives et
 63 al., 2015). However, this empirical approach often leads to overuse and misuse of antibiotics,
 64 highlighting the problem of antimicrobial resistance and raising concerns for public health
 65 (consumers), animal welfare, and environmental management.

66 As modelling gains prevalence among policy makers in animal health (Sébastien Picault et al., 2024;
 67 Pauline Ezanno et al., 2022) or plant disease (Véronique Bellon-Maurel et al., 2022; Samuel Soubeyrand
 68 et al., 2024), modelling approaches have been increasingly viewed as a way to ensure that optimal
 69 decisions are taken based on evidence-based information. Modelling has become a tool for
 70 quantifying disease transmission, predicting outbreaks, and optimizing intervention strategies.
 71 Mathematical models provide a rigorous framework for integrating biological, environmental, and
 72 management factors, facilitating evidence-based decision-making (N. Cunniffe et al., 2020). In fact,
 73 some articles strongly argue that mathematical modelling is the best method for studying and
 74 understanding the spread of BRD (Pauline Ezanno et al., 2020), they allow interdisciplinary
 75 collaboration (inputs from epidemiologists, veterinarians, farmers...), they provide a framework to
 76 describe the multiscale interactions between hosts, pathogens and the environment; they allow the
 77 simulation of various scenarios such as the impact of control measures making them indispensable
 78 for proactive disease management. Numerous mechanistic models of BRD have been proposed to
 79 investigate the spread of BRD and the factors that impact the dynamics and transmission of its
 80 infectious pathogens (Baptiste Sorin et al., 2023; Sébastien Picault et al., 2022). Due to the high
 81 complexity implied in the mechanism of BRD spread, commonly used mathematical models for
 82 BRD vary widely in their level of detail and model structure. In addition to the difference in
 83 pathogen transmission mechanisms, co-infection mechanisms and detection from clinical signs
 84 mechanisms are not yet completely understood, therefore models are still being researched and build

85 with different assumptions. Comparative modelling is a way to ensure that forecasting efforts and
86 the evaluation of intervention strategies are conserved across the range of realistic model structures
87 (R. Meza et al., 2014; Elizabeth C. Lee et al., 2018). Three related concepts are useful to consider
88 in these efforts – First, model identifiability, addresses whether the parameters of a given model can
89 be uniquely estimated from available data which is critical, particularly for models having multiple
90 parameters and an intractable likelihood. Second, model distinguishability which is closely related
91 to model identifiability addresses whether competing models can be differentiated based on their
92 ability to fit empirical data (E. Walter et al., 1984) here the challenge lies in ensuring that models,
93 while potentially similar in structure, produce sufficiently distinct predictions or outcomes. Finally,
94 Decision impact assessment, addresses the practical consequences of model-based
95 recommendations. Beyond theoretical model distinguishability, it is essential to evaluate whether a
96 selected model leads to actionable and economically viable control strategies. A well-identified
97 model should not only reproduce observed outbreaks but also yield measurable benefits – such as
98 reduced antibiotic use, improved animal welfare, and increased farm profitability. This aligns with
99 recent advances in computational epidemiology, which emphasize the integration of decision-
100 theoretic principles in model selection (stevens et al., 2023).

101 In this study, we examine the effects of model structural differences on symptomatic outbreak
102 dynamics, considering three pathogen-specific BRD mechanistic models. Our goal is to determine
103 which model best explains a theoretically observed outbreak and, in doing so, identify the infectious
104 agent responsible for the disease. We then assess the practical relevance of this identification by
105 computing the expected economic impact of pathogen-informed interventions, quantifying the
106 average benefits of targeted antibiotic treatments based on model predictions. The selected models,
107 among the most recent and realistic in the literature, share a common individual-based, discrete-
108 time, and stochastic framework, originally developed to assess the influence of batch formation
109 policies on BRD transmission. Given their intractable likelihoods, we rely on numerical exploration
110 rather than explicit structural inference, allowing us to evaluate both distinguishability and
111 identifiability while systematically investigating all plausible epidemiological scenarios based on
112 individual risk-levels. This work is conducted from a theoretical perspective to validate the proposed
113 methodology, ensuring its robustness before potential application in real-world settings.

114 By integrating epidemiological modelling with economic assessment, this study not only advances
115 methodological approaches for pathogen inference but also provides a quantitative framework for
116 evaluating the financial trade-offs of model-driven decision-making. This work contributes to the
117 broader discourse on model selection in epidemiological modelling, offering a methodology that
118 balances modelling rigor, epidemiological relevance, and bio-economic feasibility.

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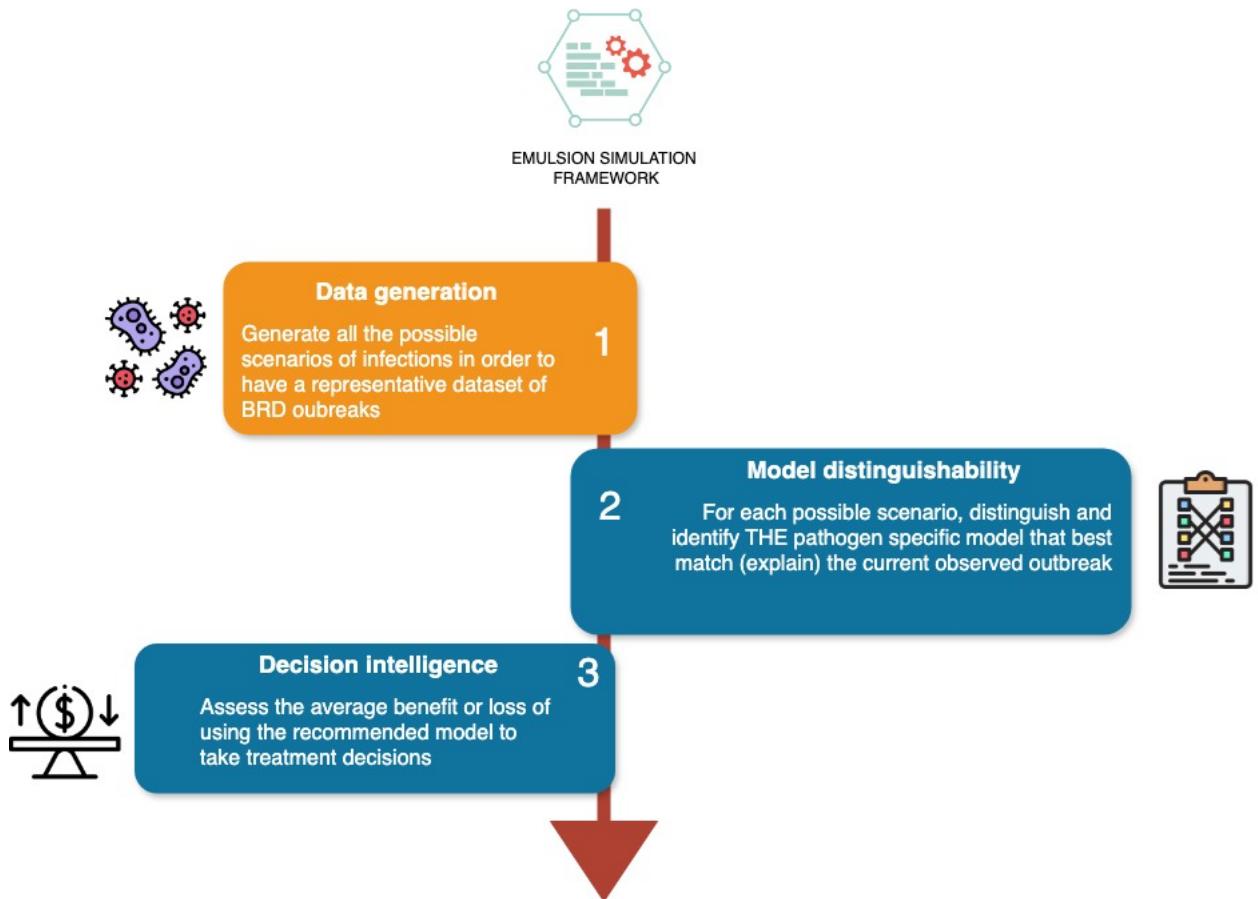
122 **2. Materials and methods**

123 **2.1. Overview of the methodological approach**

124 In this study, the three mechanistic models for BRD we focused on were originally developed and
125 published by (Sorin et al., 2023) and are described in section 2.2. Each model is tailored to one

126 of the most predominant pathogens: Orthopneumovirus bovis(BRSV), *Mannheimia*
127 *haemolytica* (Mh), *Mycoplasmopsis bovis* (Mb).

128



129

130 **Figure 1: Overview of the methodological approach.** The figure emphasizes a closed-loop
131 approach: generate diverse outbreak scenarios, identify the best explanatory pathogen model,
132 confirm that model's parameters can reliably be inferred, and finally evaluate the
133 bioeconomic or operational impact of using these model-based insights in real-world
134 settings.

135

136 EMULSION (Picault et al., 2019b) is a simulation framework designed to address the limitations
137 of traditional epidemiological models by enhancing flexibility and transparency in modelling complex
138 systems. It enables easier collaboration among different experts such as veterinarians, modeller,
139 farmers. Integrated with a versatile agent-based simulation engine, processes are represented using
140 finite state machines, allowing for detailed modelling of transitions, conditions, and actions. This
141 approach facilitates interdisciplinary collaboration and adaptability.

142 In the first step (Fig. 1 – box 1), we repurposed those pathogen-specific mechanistic BRD models
143 within the Emulsion simulation framework to construct synthetic time series of outbreak dynamics.
144 Specifically, we considered three batches of $N = 12$ animals each, observed over a limited period
145 of $T = 277$ days. Let $t \in \{0, 0.5, 1, \dots, 2T\}$ (measured in days) denote discrete 12-hour timesteps,

reflecting the average frequency at which farmers typically visually assess cattle for clinical symptoms (Sébastien Picault et al., 2022). For each pathogen-specific model, key parameters $\boldsymbol{\theta}$ were systematically varied within biologically plausible ranges. For a given parameter set $\boldsymbol{\theta}_k$, we numerically solved the underlying system of equations to obtain the number of symptomatic animals at each timestep, yielding a trajectory $\{y_t^{(k)} : t = 0, 0.5, 1, \dots, 2T\}$. By aggregating these simulations over all parameter configurations $k = 1, \dots, K$, we gathered a comprehensive synthetic dataset that closely mirrors conditions in French fattening operations and captures all the plausible BRD outbreaks based on individual risk-levels. Note that these models (see section 2.2) are stochastic and incorporate random effects of the detection method (visual assessment of clinical symptoms) ensuring that inherent randomness of biological systems are conserved.

In the second step (Fig. 1 – box 2), we focused on distinguishing three pathogen-specific models – each corresponding to a different BRD pathogen – based on a limited window of synthetic outbreak data (we assessed our methodology on the initial 5 days of simulated disease). Formally, if $\{y_t\}_{t=1}^{T^*}$ denotes the synthetic time series of symptomatic animals over the first $T^* = 5$ days, we computed a goodness-of-fit measure $\mathcal{L}(\mathcal{M}_i | \{y_t\}_{t=1}^{T^*})$ for each model \mathcal{M}_i , $i \in \{\text{Brsv, Mh, Mb}\}$. By comparing the good of fit between simulated outbreak and a reference trajectory designated as “true”, we identify which pathogen-specific model best explained the early-stage outbreak dynamics. Consequently, under certain assumptions (detailed in the Discussion section), if a farmer were to record the same 5 days of observations in a real-world scenario, they could analogously select the most likely pathogen responsible for the observed clinical signs, thereby enabling more targeted control and treatment strategies.

In the third and last step (Fig. 1 – box 3), we employed the “recommended” model, calibrated using the default parameters values from the original study (Baptiste Sorin-Dupont et al., 2023), which represent the average effects of each pathogen group. This model was then used to guide disease-control decisions over the remaining 273 days. Specifically, we computed the expected profit or loss, $\mathbb{E}[\text{Profit} | \mathcal{M}_{\text{recommended}}]$, to quantitatively, assess the potential benefits of a pathogen-informed treatment decision system, including its impact on antimicrobial usage and the net profit.

173

174 2.2. Model descriptions

175 The most realistic mechanistic models are stochastic models, designed to evaluate how batch
176 composition and size influence pathogen spread and intervention outcomes (Baptiste Sorin-Dupont et
177 al., 2023). These individual-based stochastic models integrate viral and bacterial pathogens and
178 account for individual risk levels, providing insights into disease dynamics and control strategies. In
179 the paper, we employed the latter models because they are representative of the different pathogen
180 effects on the spread of BRD, ranging from acute outbreaks (BRD) to opportunistic bacterial
181 infections (*Mh*) and chronic persistence (*MB*)

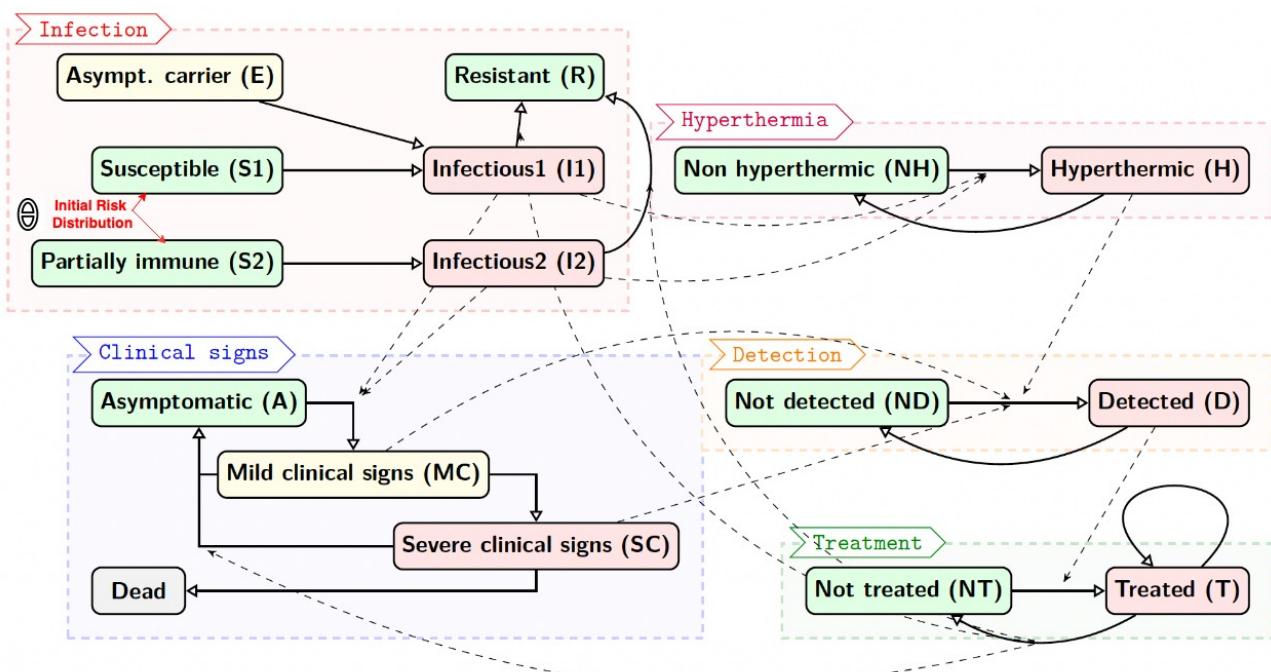
182

183 2.2.1. Orthopneumovirus bovis(BRSV) infection model

184 This model describes the transmission of BRSV (Kurucay H.N. et al., 2025), a highly contagious

185 airborne virus with rapid spread dynamics. It follows a stochastic compartmental structure, where
 186 individuals can begin as susceptible (S1, S2) and can be infected either for the first time (I1) or as
 187 reinfections (I2), with reinfected individuals exhibiting reduced infectiousness. Individuals can
 188 become asymptomatic carriers (E) before progressing to an infectious state. After infection,
 189 individuals eventually recover and transition to the resistant (R) state. Clinical states include mild
 190 clinical signs (MC), which may escalate to severe clinical signs (SC), with a probability of
 191 developing severe illness. Severe cases have a risk of mortality, leading to a transition to the dead
 192 state if the disease is too severe. Detection of diseased animals relies on clinical symptoms, with
 193 severe cases more likely to be detected. Detection leads to treatment (T), which may succeed,
 194 causing individuals to transition back to asymptomatic (A), or fail, requiring multiple rounds of
 195 treatment. Hyperthermia (H) also plays a role in detection, as infected individuals may exhibit fever,
 196 increasing their likelihood of being diagnosed. A key feature of this model is the incorporation of
 197 partial immunity.

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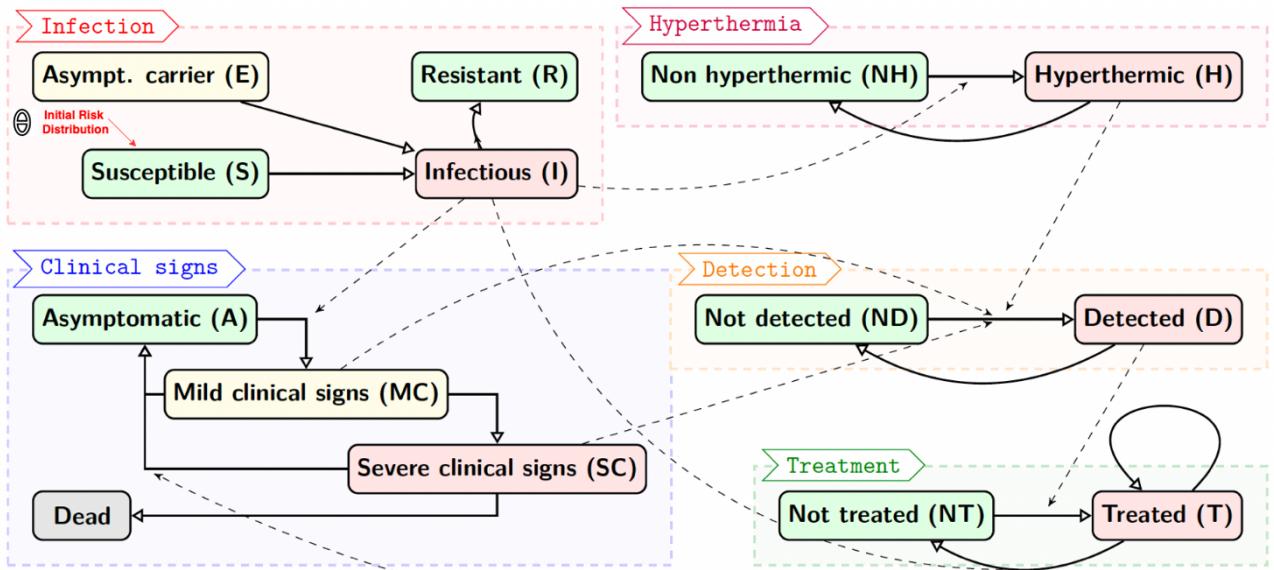
200 **Figure 2: Model overview for BRSV.** The model incorporates four processes (infection,
 201 clinical signs, hyperthermia, detection, treatment) associated to individual states (rounded
 202 boxes), which could evolve themselves (plain arrows) but also influenced each other (dashed
 203 arrows). Figure adapted from (Baptiste Sorin-Dupont et al., 2023).

204

205 2.2.2. *Mannheimia haemolytica* (Mh) infection model

206 This model represents the transmission of *Mh* (Mohamed R.A et al., 2008), a bacterial pathogen
 207 with opportunistic behaviour, often colonizing the respiratory tract before causing disease under
 208 stress-induced immunosuppression. The model includes susceptible (S) individuals who may

209 transition into asymptomatic carriers I before becoming infectious (I). unlike BRSV, there is no
 210 reinfection state, as infection leads to either clearance or severe disease. The progression of clinical
 211 signs follows the same patterns as for the BRSV model. Severe cases may either recover, die, or
 212 be detected and treated (T). Detection of diseased animals occurs through clinical observation and
 213 hyperthermia (H), which increased detection probability. Treatment is also modelled in the same
 214 way as for BRSV model.



215
 216 **Figure 3: Model overview for *Mh* & *Mb*.** The model incorporates four processes (infection,
 217 clinical signs, hyperthermia, detection, treatment) associated to individual states (rounded
 218 boxes), which could evolve themselves (plain arrows) but also influenced each other (dashed
 219 arrows). Figure adapted from (Baptiste Sorin-Dupont et al., 2023).

220 221 2.2.3. *Mycoplasmopsis bovis* (*Mb*) infection model

222 The third and last model (*Mb*) incorporated chronic infection dynamics, characterized by a slow-
 223 spreading, long-term colonizing bacterial pathogen causing intermittent clinical signs (Bürki S. et
 224 al., 2015). The states machines describing the infection mechanisms of *Mb* (Infection, clinical signs,
 225 hyperthermia, detection, treatment) are identical to those of *Mh*. However, unlike *M. haemolytica*,
 226 nominal values of the parameters of *M. bovis* are such the model expresses long-term persistence,
 227 with some infectious individuals (I) failing to recover fully, remaining chronic carriers. Detection
 228 is particularly challenging, as *Mb* infections can be subclinical for extended periods (Maunsell F.P.
 229 et al., 2009), making early diagnosis unreliable. In this model, infection durations are prolonged.
 230 The model is well-suited for studying persistent infections. The structure of this model is identical
 231 to that of *Mh* and is represented in figure 3.

234

2.3. Generating BRD outbreak scenarios

235

2.3.1. Models' baseline parameters

236

Each epidemiological simulation starts with a predefined initial condition, which specifies the composition of the batch in terms of individual risk levels. Let $\theta = (\theta_L, \theta_M, \theta_H)$ (Fig. 2 & 3) with the constraints $\theta_L, \theta_M, \theta_H \in [0, 1]$ such that $\theta_L + \theta_M + \theta_H = 1$. Where θ is a vector representing the proportion of individuals in each risk category and $\theta_L, \theta_M, \text{and } \theta_H$ denote the fractions of low, medium, and high-risk individuals in the population respectively. These proportions are essential for defining the starting point of the simulations, as they determine the susceptibility and transmission potential within a group. The effects of θ are pathogen-dependent. Highly contagious viruses such as BRSV exhibit rapid spread dynamics, whereas opportunistic bacterial infections like *Mh* are more influenced by host immunity and stress-related susceptibility. Chronic pathogens such as *Mb* could depend heavily on θ_H , as the persistence of infected individuals in the population prolongs transmission and sustains pathogen circulation. The structure of θ thus dictates outbreak intensity, disease persistence, and the effectiveness of control interventions, making it a crucial parameters vector in the modelling of BRD dynamics. While these parameters are the most important, they are common across all models. Additional information on specialized parameters for each model can be found in the original paper published (Baptiste Sorin et al., 2023).

252

253

2.3.2. Reference synthetic outbreak scenario generation

254

To mimic the average settings in real fattening farms in France, we considered 1 batch composed of 12 animals. Given that risk levels are discrete and partitioned into three categories, for N=12, the number of batch composition follows a combinatorial constraint and results in a total of 91 distinct settings. The number of valid allocations can be derived using the stars and bars theorem, where N identical objects (animals) are distributed into $k = 3$ and S serves as the space of initial conditions for the simulations. Increasing N (the total number of animals) would expand the space S exponentially, making simulations computationally more demanding. Each $\theta \in S$ was used as an initial condition for each of the three pathogen-specific mechanistic models $\mathcal{M}_i = \{\text{Brsv, Mb, Mb}\}$, however since these models are stochastic, running the same model on the same parameters will yield slightly different results. To capture this variability that is also present in the real-world, we made sets of repetition ($r = 50$) for each combination of $\theta \in S$: $\mathcal{M}_i(\theta_j)^{(k)}$ with $k = 1, \dots, r$. Each repetition is then used as input for the mechanistic models. Thus, for each (θ, \mathcal{M}) pair, we conduct r independent runs. The choice of $r = 5$ repetitions is a reasonable trade-off that balances computations efficiency and results stability. Each simulation produced a trajectory over time for each state variable defined in the model description section, including the observed symptomatic individuals. Thus, the final dataset consisted of: $|S| \times |\mathcal{M}| \times r = 91 \times 3 \times 50 = 13650$ simulated realistic BRD outbreaks, 150 cases (3 pathogens \times 50 répétitions) for each of the 91 initial conditions. All model simulations and computations were done using Python 3.8 and using Emulsion simulation engine (Version 1.2rc6).

273

Algorithm 1 Simulation Design for Synthetic Dataset

```
1: Define experimental setup:
2: Set batch size  $N = 12$ .
3: Compute the set  $\mathcal{S}$  of valid risk allocations using the combinatorial formula.
4: Define the set of mechanistic models  $\mathcal{M} = \{M_{\text{BRSV}}, M_{\text{MH}}, M_{\text{MB}}\}$ .
5: Set the number of repetitions  $r = 50$ .
6: for each initial risk composition  $\boldsymbol{\theta}_j \in \mathcal{S}$  do
7:   for each pathogen model  $M_i \in \mathcal{M}$  do
8:     for each repetition  $k = 1, \dots, r$  do
9:       Initialize empty set  $\mathcal{O}$  for storing stochastic outputs.
10:      Simulate model  $M_i(\boldsymbol{\theta}_j)^{(k)}$  to obtain trajectory  $O_k$ .
11:      Store  $O_k$  in  $\mathcal{O}$ .
12:    end for
13:  end for
14: end for
15: Finalize dataset:
16: Aggregate all trajectories into structured dataset.
17: The final dataset contains  $|\mathcal{S}| \times |\mathcal{M}| \times r$  simulations.
```

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Algorithm 1: Simulation setup for synthetic data generation. A batch of 12 young calves was partitioned into 91 possible combinations of initial risk levels. Each combination was fed with repetition into 3 pathogen-specific mechanistic models, with 50 stochastic & independent runs per model. In total, 13 650 simulation points were generated to generate biophysical-driven dynamics.

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2.4. Inverse modelling – Distinguishing & recognizing BRD infectious agents from observations

283 Model distinguishability refers to differentiating between competing models in a theoretical setting,
284 as opposed to model selection, which applies when working with real-world data. Since we do not
285 analyse the analytical form of these models but instead solve them numerically, our approach falls
286 under numerical distinguishability. This distinction is crucial, as it allows us to systematically assess
287 key hypotheses and evaluate the theoretical structure of these models without the logistical
288 constraints of setting up a full-scale experimental study with veterinary observations. Given an
289 observed outbreak S^* , the objective of model distinguishability is to identify the model \mathcal{M}_i that
290 best explains the observations: $\hat{M} = \arg \max_{M_i \in \mathcal{M}} P(M_i | S^*)$. Where $P(M_i | S^*)$ represents the posterior
291 probability of model \mathcal{M}_i given the observed summary statistics S^* . However, the likelihood function
292 $P(M_i | S^*)$ is intractable for the BRD models under consideration partly due to their stochastic nature
293 and high-dimensional latent space. Consequently, we relied on likelihood-free inference methods,
294 notably the Approximate Bayesian Computation (ABC) (Beaumont et al., 2019), that bypasses
295 explicitly likelihood evaluation.

296 Instead of directly computing the likelihood $P(\mathbf{S}^*|\theta)$, ABC relies on simulating data under different
 297 parameter values and comparing the resulting summary statistics with the observed data. The key
 298 idea is to sample parameters θ from a prior distribution, generate synthetic data using a mechanistic
 299 model, and compute a distance metric between simulated summary statistics \mathbf{S} and observed
 300 summary statistics \mathbf{S}^* . Parameter values yielding summary statistics within a predefined tolerance
 301 ε are retained, forming an approximation of the posterior distribution $P(\theta|\mathbf{S}^*)$.

302 Approximate Bayesian Computation also enables model distinguishability when the likelihood
 303 function is intractable. We use model indicator $i = \{ \text{BRSV}, Mh, Mb \}$ which represent the set of
 304 candidate models $\mathcal{M} \in \{\text{BRSV}, Mh, Mb\}$. We sample $i \sim \pi(I)$ from the prior distribution over
 305 models and treat it as a categorical variable in the ABC framework. After generating simulated
 306 summary statistics (vector composed of symptomatic dynamics) for each model, we apply
 307 multinomial logistic regression to estimate the posterior probability $P(I = i|\mathbf{S} = \mathbf{S}^*)$ (Fagundes et
 308 al., 2007). We make the regression estimate locally around \mathbf{S}^* in the same way as in the standard
 309 ABC approach using the same summary statistics as in (Eyango et al., 2024), specifically only the
 310 top 10% simulations closest to the observations are retained, and these are weighted by a gaussian
 311 kernel.

312 Every single outbreak from the 1365 realistic BRD outbreaks simulated in the previous section (cf.
 313 *Reference synthetic outbreak scenario*) was regarded as the true observations in the ABC framework
 314 and model distinguishability was performed on them. Our dataset consists of systematically varied
 315 initial conditions per model with 50 repetitions per condition, it provides a uniform representation
 316 of all possible discrete outbreak initial compositions.

Algorithm 2 Distinguishing BRD pathogen-specific mechanistic models

- 1: **Input:** Set of observed outbreaks S^* , candidate models \mathcal{M} , prior distributions $\pi(\theta)$, repetitions r
- 2: **Output:** Inferred model $\hat{\mathcal{M}}$, classification accuracy \mathcal{A} , and performance metrics
- 3: **for** each observed outbreak S_j^* **do**
- 4: **for** each candidate model \mathcal{M}_i **do**
- 5: **for** each repetition $k = 1, \dots, r$ **do**
- 6: Sample parameters $\theta_i^{(k)} \sim \pi(\theta)$
- 7: Simulate summary statistics $\mathbf{S}_i^{(k)}$ from $\mathcal{M}_i(\theta_i^{(k)})$
- 8: Retain top 10% closest $\mathbf{S}_i^{(k)}$ to \mathbf{S}_j^* using distance metric $d(\mathbf{S}, \mathbf{S}^*)$
- 9: Apply Epanechnikov kernel weighting to retained simulations
- 10: Perform multinomial logistic regression to estimate $P(\mathcal{M}_i|\mathbf{S}_j^*)$
- 11: Get $\hat{\mathcal{M}}_j = \arg \max_i P(\mathcal{M}_i|\mathbf{S}_j^*)$
- 12: Compute overall classification accuracy:

$$D_j = \frac{1}{r} \sum_{k=1}^r \mathbf{1}(\hat{\mathcal{M}}_j^{(k)} = M_j)$$

- 13: Compute additional performance metrics: Sensitivity ...
- 14: **end for**
- 15: **end for**
- 16: **end for**

318
319
320 **Algorithm 2:** model distinguishability using Approximate Bayesian Computation with
multinomial logistic regression. This process outputs the inferred pathogen-model and the
performance metrics, such as the accuracy.

321 This distinguishability index (accuracy) measures the proportion of cases where the selected model
322 matches the true model and varies in the range [0,1], higher values indicate better distinguishability
323 among models. To get even further, since model distinguishability is inherently a classification
324 problem, we further evaluate performance using standard classification metrics, particularly:

325 Table 1: Distinguishability performance metrics

Metrics	Formula	Description
True Positive Rate (Sensitivity or Recall)	$TPR_{M_i} = \frac{TP_{M_i}}{TP_{M_i} + FN_{M_i}}$	Probability of correctly identifying the true pathogen. Important for ensuring correct treatment when the pathogen is actually present
False Positive Rate (1 – Specificity)	$FPR_{M_i} = \frac{FP_{M_i}}{FP_{M_i} + TN_{M_i}}$	Probability of wrongly assigning a pathogen when it is not present. Important for estimating the cost of inadequate control measures
Positive Predictive Value (Precision)	$PPV_{M_i} = \frac{TP_{M_i}}{TP_{M_i} + FP_{M_i}}$	Probability that a predicted pathogen is actually the correct one. Useful for guiding confidence in the decision
Negative Predictive Value	$NPV_{M_i} = \frac{TN_{M_i}}{TN_{M_i} + FN_{M_i}}$	Probability that a rejected pathogen is actually absent. Important for minimizing unnecessary treatments.

326 The full distinguishability procedure was conducted in R programming language, using the ABC
327 package (version 2.2.2; [Csilléry et al., 2012](#)).

328

329 2.5. *Bioeconomic impact - Expected profit/loss of pathogen-informed treatments*

330 2.5.1. *A simple economical model*

331 The economic model used in this study was inspired by a veterinary thesis ([Théo Salles, 2024](#)) on a
332 mechanistic model of BRD and by insights from an “Inosys Réseaux Elevage” report ([Benoteau G.
333 et al., 2023](#)). In particular, Inosys’ case type methodology, which reconstructs representative farm
334 systems through collective modelling and field expertise.

335 The economic model developed evaluates the net profit at the end of the fattening period by
336 calculating the difference between total revenues generated from cattle sales and the direct costs
337 incurred during the fattening process. This approach is a simplified version, which excludes indirect
338 costs, focusing solely on tangible, easily measurable expenditures and earnings directly linked to
339 animal health and fattening performance. The net profit (Δ) is defined as: $\Delta = R - C$ (1). Where R
340 represents the total revenues from cattle sales and C denotes the total costs. Total revenues R are
341 calculated based on the sale of fattened cattle, taking into account the carcass weight and conformation
342 grade influenced by the health status during the fattening period and costs C include purchase costs

343 of calves, feed costs, medical treatment costs, and veterinary services' costs.

344 The purchase costs are computed as: $C_{purchase} = N_{calf} \cdot P_{calf}$ (2). Where N_{calf} is the total number
345 of calves purchased by the farmer, and P_{calf} is the price per calf. The purchase price of a calf in is
346 1185€, it is the average price used in typical Charolais fattener farms in Brittany published by "Inosys
347 réseaux d'élevage" (Benoteay G. et al., 2023).

348 The feed costs primarily represent the feeding expenses of animals, calculated as: $C_{production} =$
349 $F_{cost} \cdot \sum WG_{status}$ (3). Where WG_{status} is the cumulative weight gain (depending on the clinical
350 status \in asymptomatic, mild, severe) of all the animals by the end of fattening period, and F_{cost}
351 represents the feed cost per kilogram, set at €0.9 per kg of live weight. The cumulative weight gain is
352 a function of daily weight gain (GMQ) and the durations of the fattening period (D), expressed as:
353 $WG_{status} = GMQ_{status} \cdot D$. The average fattening period (D) in France is estimated at 277 days (Théo
354 Salles, 2024). The GMQ values vary depending on the animal's health status: 1.388 kg/day for
355 asymptomatic, 1.080 kg/day for mild cases, and 0.925 kg/day for severe cases (Benoteau G. et al.,
356 2023). For healthy animals. The decline in GMQ was calculated by Blakebrough-Hall (Blakebrough-
357 Hall C et al., 2020) on Charolais et also by Théo Salles (Théo Salles, 2024)

358 Treatment costs are determined by the number of individual treatments administered (antibiotics) and
359 the cost per treatment: $C_{treatment} = N_{doses} \cdot P_{treatment}$ (4). Where N_{doses} is the total number of
360 antibiotic doses administered by the end of fattening period, and $P_{treatment}$ is the unitary price of
361 antibiotics set at an average of €13 (Théo Salles, 2024).

362 The cost of veterinarian services is calculated based on the time taken to administer individual
363 antibiotic and the hourly price of veterinary services: $C_{veterinary} = N_{doses} \cdot t_{treatment} \cdot P_{veterinary}$
364 (5). Where N_{doses} is the total number of antibiotic doses administered by the end of fattening period,
365 $t_{treatment}$ is the average time spent to perform an individual antibiotic treatment estimated at 40 min
366 (0.67 hours) (Wang et al., théo salles, 2024), $P_{veterinary}$ is the hourly veterinary price estimated at
367 €9.94 in France from the Convention Collective Nationale Agricole (CCNA).

368 Revenue from cattle sales is influenced by the carcass weight and conformation grade by the end of
369 the fattening period which are dependent on the animal's health status during fattening. The total
370 carcass weight is computed as: $CW_{status} = N_{status}^{alive} \cdot (W^0 + WG_{status}) \cdot CY$. Where N_{status}^{alive} is the
371 number of alive cases per clinical status. Note that for individuals that died during the fattening period,
372 their buying and feed costs and kept (they increase the costs), however for the selling, they were
373 subtracted. W^0 is the initial weight of an animal and WG_{status} is the weight gained (depending on
374 the clinical status) by an animal by the end of fattening period as defined above and CY is the carcass
375 yield (estimated at 0.58) that allows to convert live weight into carcass weight for young beef
376 Charolais (Lefrand I et al., 2019). That formulation supposes that all the calves are bought with the
377 same weights. The conformation quality (Table 2) refers to the muscle development and shape of an
378 animal's carcass, which affects its market prices and is graded from high (U) to lower (R) (Duflot B.,
379 2023; These de Joly; Théo Salles, 2024).

380

381

382 Table 2. Impact of health status on carcass conformation and sale price

Conformation	Price	Proportions
--------------	-------	-------------

		Asymptomatic	Mild signs	Severe signs
R	5.25 €/kg	20%	60%	100%
U	5.41 €/kg	40%	40%	0%

383

384 The sales revenue is a weighted sum of these factors, reflecting the impact of health status on carcass
 385 quality and market price: $R_{sales} = CW_{status} \cdot (Prop_{status}^R \cdot (P_R - P_U) + P_U)$ (6). Where $Prop_{status}^R$
 386 is the proportion of conformation R (table xx) depending on their clinical status, P_R and P_U are the
 387 slaughter price of animals in conformation R and U.

388 Thus, the economic model (Δ) in Eq. (1) can be detailed as:

$$389 \Delta = N_{status} \cdot [W^0 + (GMQ_{status} \cdot D)] \cdot CY \cdot (Prop_{status}^R \cdot (P_R - P_U) + P_U) - N_{calf} \cdot P_{calf} - \\ 390 F_{cost} \cdot \sum(GMQ_{status} \cdot D) - N_{doses} \cdot (P_{treatment} - t_{treatment} \cdot P_{veterinary}) \quad (7)$$

391 Our simplified economic model operates under the assumption that weight loss due to disease is
 392 exclusively related to the time spent in diseased states (mild and severe). At the end of the fattening
 393 period, all the animals are sold at the same time: No special interventions are made to compensate for
 394 weight loss; feed costs and weight gain are considered linear, unaffected by other environmental or
 395 management factors. Our net profit is calculated only during the fattening period, and therefore is not
 396 the same as the net profit of the farm. The net profit we computed is related to beef bovine fattening
 397 and BRD control measures meanwhile the farm net profit is a larger notion that includes for instance,
 398 costs of energy, buildings, and government aid.

399

400 2.5.2. Integration with Mechanistic models

401 In this subsection, we describe the integration of mechanistic BRD models with our economic model.
 402 The mechanistic models simulate the progression of BRD at the individual animal level, generating
 403 outputs that reflect the dynamics (infection, clinical signs, detection, treatment) over time. These
 404 outputs are essential for translating biological processes into quantifiable economic impacts, such as
 405 weight gain, feed efficiency, and treatment costs. Default outputs are described in model description
 406 subsection (see 2.2), additional outputs required to run our economic model are described in table 3:
 407

408 Table 3: Table of Key variable linking mechanistic outputs to economic inputs

Mechanistic model output	Description	Impact
Asymptomatic count	Number of asymptomatic animals detected by the end of the fattening period	Healthy animals maintain higher daily weight gain, leading to increased sale weights and quality (conformity)
Mild count	Number of animals detected presenting mild clinical signs	Reduced feed efficiency increases costs while lowering final weight
Severe count	Number of animals detected presenting clinical signs	Severe cases drastically reduce weight gain and increase feed inefficiencies
Dead	Total number of dead animals	They increase the costs (buying, feed,

antibiotics), and decrease the sells (no revenue from them)

Treatment doses	Cumulative number of doses administered	-
Batch size	Number of animals per batch (batches have an equal number of individuals)	-
Batch number	Number of batches	-

409

410

411

412 *2.5.3. Estimating the expected profit/loss*

413 The objective of computing the expected profit or loss is to quantify the financial impact of decision
 414 errors in pathogen identification. To quantify the expected profit or loss resulting from model-informed decisions, we define a random variable Π representing the net profit (cf. 2.5.1) associated
 415 with pathogen identification outcomes. The decision-making process can lead to four possible
 416 outcomes: correctly identifying bacterial infections (B^+), incorrectly diagnosing a viral infection as
 417 bacterial (V^+), incorrectly diagnosing a bacterial infection as viral (B^-), and correctly identifying viral
 418 infections (V^-). Each of these outcomes influences both treatment decisions and their financial
 419 consequences. Let \mathcal{X} be a discrete random variable representing the outcome of pathogen
 420 identification, taking values in the set $\{B^+, B^-, V^+, V^-\}$. The probability mass function $P(\mathcal{X}=x_i)$
 421 corresponds to the proportion of each outcome in the confusion matrix. For instance, comparing
 422 bacteria to virus in our case (Table 4):
 423

424

425

Table 4: Confusion matrix. Illustrates the four possible outcomes for antibiotic treatment decisions

		Relevance of antimicrobial treatment	
		Needed	Not needed
Decision	treatment	Correctly identifying bacterial infections ($B^+ = \text{Correct recommendation}$)	Incorrectly identifying a viral infection as bacterial ($V^+ = \text{False alarm}$)
	no treatment	Incorrectly identifying a bacterial infection as viral ($B^- = \text{Missed opportunity}$)	Correctly identifying viral infections ($V^- = \text{Correct rejection}$)

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The default decision rule is that any animal exhibiting clinical signs is systematically treated. This approach leads to two possible outcomes: either the animal is truly infected with a bacterium and receives antibiotic treatments (B^+), or it is infected with a virus yet receives antibiotic treatments (V^+). Without prior information about the true prevalence of pathogens, the expected net profit under this rule is calculated as the simple average of the net profits associated with these two outcomes:

$$E[\Delta]_{\text{default}} = \frac{1}{2} [\Pi(B^+) + \Pi(V^+)].$$

In contrast, if the treatment is tailored to the pathogen type, the decision process distinguishes among four outcomes: B^+ , B^- , V^+ , V^- . The expected profit $E[\Delta]_{\text{informed}}$ is then calculated as:

435
$$E[\Delta]_{\text{informed}} = \sum_{x \in \{\text{B+}, \text{B-}, \text{V+}, \text{V-}\}} P(X = x) \cdot \Pi(x)$$

436
437 where $\Pi(x)$ denotes the net profit as computed in the previous part (2.5.1) associated with outcome
438 x . The probabilities of each event can be computed as: $P(X = x) = \frac{N_{X=x}}{N_\Omega}$ where $N_{X=x}$ is the count
439 of outcomes for event x and N_Ω is the total number of cases in the sample space Ω . Assuming that
440 the benefits of correct treatment and the cost savings from avoiding unnecessary treatments outweigh
441 the losses incurred from mis-identification.

442
443
444 *2.5.4. Case study: 5 days of observing before taking a treatment decision*

445 To illustrate the application of our methodology, we conducted a case study. Imagine a situation
446 where a BRD outbreak occurs in beef cattle farm managing one batch of 12 animals. At the onset
447 of the outbreak, the farmer has no prior information regarding the nature of the infectious agent.
448 The only observable metric for the farmer is the number of symptomatic animals detected daily.
449 However, due to non-specificity of clinical signs and the tendency of some animals to conceal
450 symptoms, the observed number of symptomatic cases is consistently lower than the actual number
451 of infected animals.

452 For five consecutive days, the farmer records the total number of symptomatic animals detected
453 each day. This limited dataset is then employed in our methodology to distinguish and infer the
454 most probable pathogen-model responsible for the outbreak. Based on the inferred pathogen, we
455 recommend specific control measures: If the pathogen is identified as bacterial, we advise treating
456 the detected symptomatic animals with antibiotics. And if the pathogen is viral, we recommend not
457 treating, as antibiotics would be ineffective.

458 The pathogen-specific model is subsequently used to forecast the progression of the disease for the
459 remainder of the fattening period. In France, the fattening period for beef cattle typically can last
460 until the animals reach up to 24 months of age ([Théo Salles, 2024](#)). This forecast provides insights
461 into the expected trajectory of the outbreak, including potential weight loss, treatment needs, and
462 overall animal health impacts.

463 We then integrated these forecasts into our economic model to estimate the expected profit or loss
464 under the recommended intervention strategy. This process allows us to assess the financial
465 implications of model-driven decision-making. Furthermore, this methodology was applied to all
466 the BRD outbreak scenarios generated (see [Section 2.3.2](#)). By evaluating the expected profit and
467 loss across diverse epidemiological conditions, it enable to comprehensively assess the profitability
468 and robustness of our pathogen identification method, ensuring its applicability and effectiveness
469 in real-world outbreak situations.

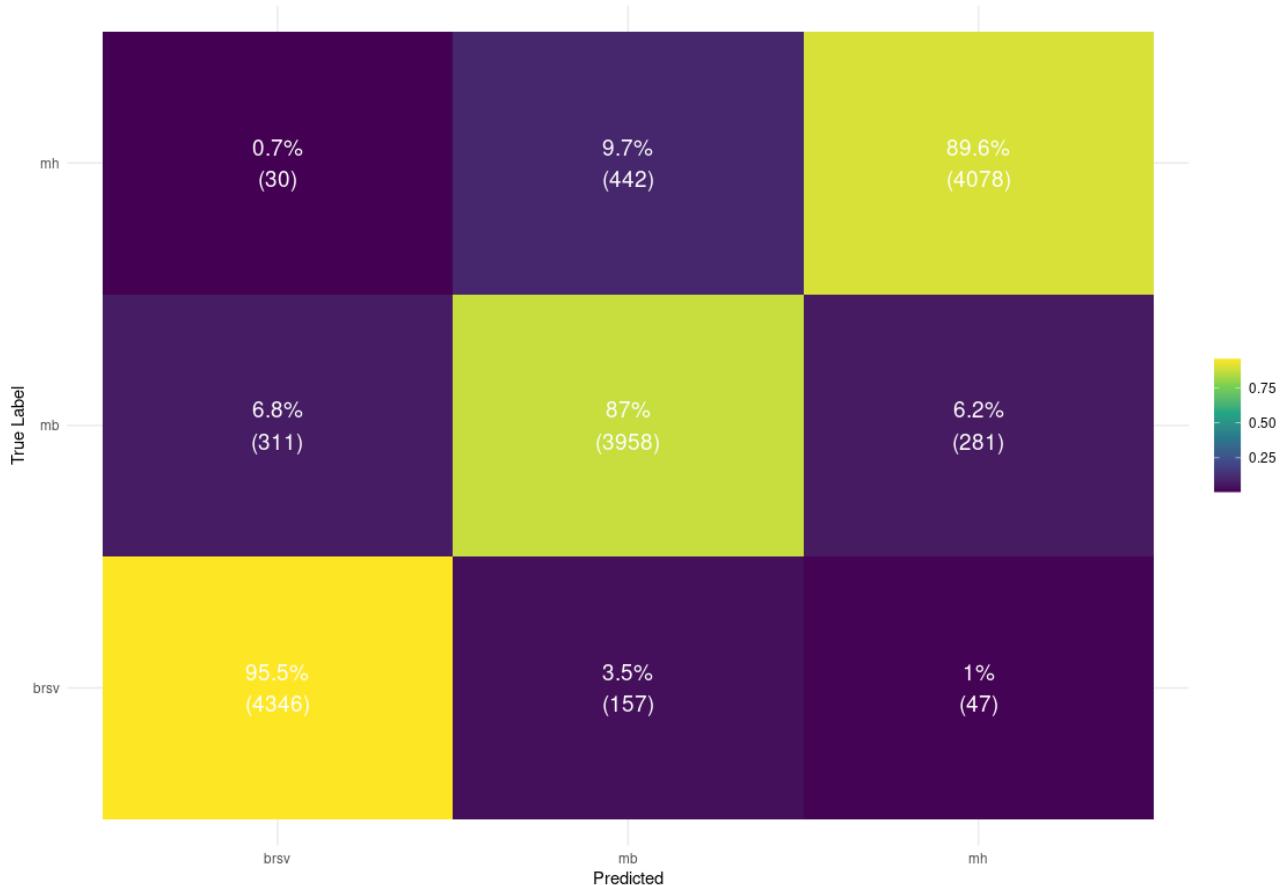
470
471

3. Results

472 *3.1. BRD Model distinguishability - a BRD infectious agent identification method*

473 *3.1.1. Performance assessment*

474



475
 476 Figure 4: Confusion matrix. Classification performance for BRSV, *Mh* and *Mb*. The
 477 diagonal represents correctly classified instances, while off-diagonal values indicate
 478 misclassifications between classes.

479
 480
 481
 482
 483 Table 5. Pathogens identification performances

Metrics	BRSV	<i>Mb</i>	<i>Mh</i>
True Positive Rate	0.96	0.87	0.90
False Positive Rate	0.04	0.07	0.04
Positive Predictive Value	0.93	0.87	0.93
Negative Predictive Value	0.98	0.93	0.95
Balanced Accuracy	0.96	0.90	0.93
Support	4550	4550	4550

484

485 We evaluated the capability of our methodology to distinguish among three BRD-causing
 486 pathogens, Orthopneumovirus bovis (BRSV), *Mannheimia haemolytica* (*Mh*), and *Mycoplasmopsis*
 487 *bovis* (*Mb*) using synthetic symptomatic trajectories recorded over the first five days of an outbreak.
 488 Our analysis is based on a confusion matrix (Figure 4) and key classification metrics presented in

489 **Table 5**, which include the true positive rate (TPR), positive predictive value (PPV), and false
 490 positive rate (FPR).

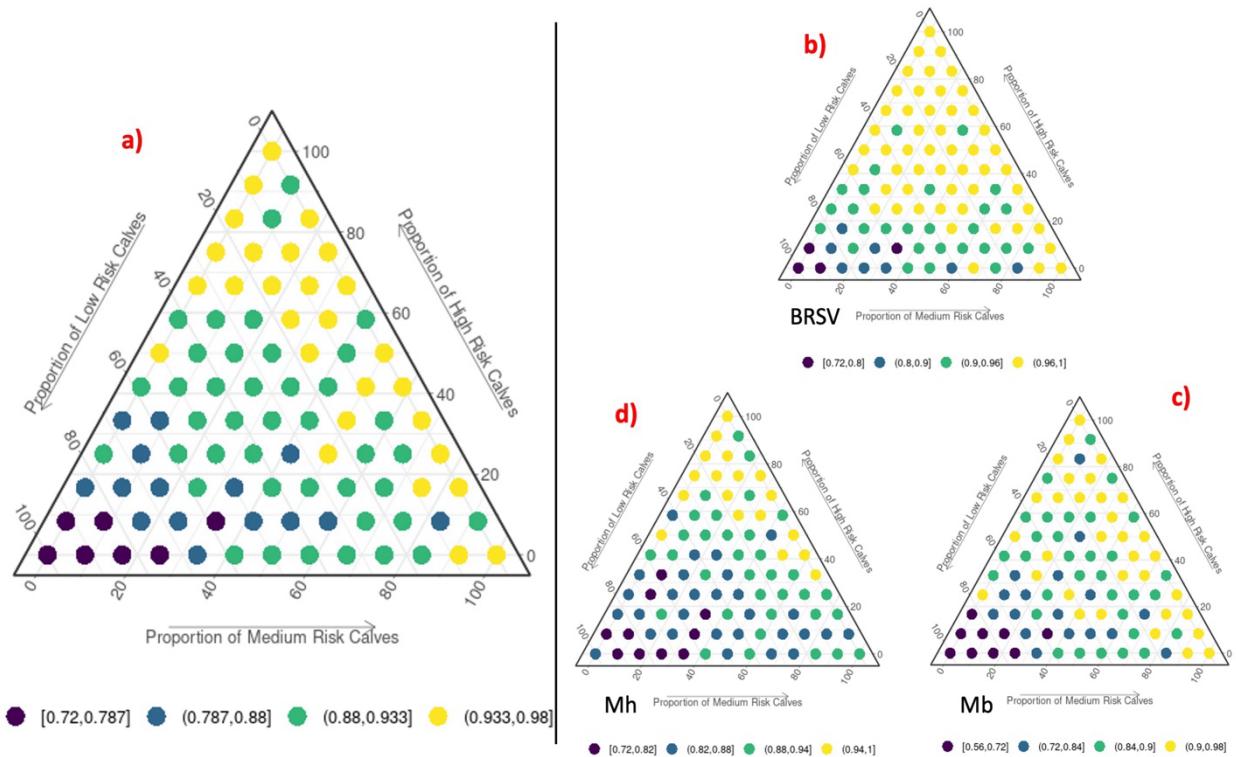
491 Distinguishing BRSV model amongst other models demonstrated the highest performance,
 492 achieving a TPR of 96% and a PPV of 93%, with an FPR of only 4%. These metrics indicate that
 493 the symptomatic progression associated with BRSV is distinct enough to allow for reliable
 494 identification, with minimal misclassification. When errors did occur, BRSV cases were primarily
 495 confused with Mb (3.5%), suggesting a minor overlap in their symptom profiles.

496 In contrast, the *Mh* model displayed a TPR of 90% and a PPV of 93%. However, about 9.7% of *Mh*
 497 cases were misclassified as Mb, which implies that the symptomatic trajectories of these bacterial
 498 infections share certain similarities that challenge precise differentiation. Mb itself was the most
 499 difficult to classify, with both a TPR and PPV of 87%. Misclassification for Mb was higher, with
 500 6.2% of cases being mistaken for *Mh* and 6.8% for BRSV, highlighting the subtle nature of its
 501 symptomatic signal.

502 Overall, the framework achieved robust classification performance for BRSV and *Mh*, while the
 503 identification of Mb presented additional challenges due to overlapping symptom dynamics.

504

505 3.1.2. Pathogen identification according to batch configurations



506

507 Fig 5: Pathogen distinguishability map after 5 days of observing of symptomatic dynamics. They
 508 represent the balanced accuracy of pathogen identification as a function of batch initial risk
 509 composition. The large ternary plot on the left is the overall classification accuracy. And on the right
 510 are the specific accuracies of each pathogen.

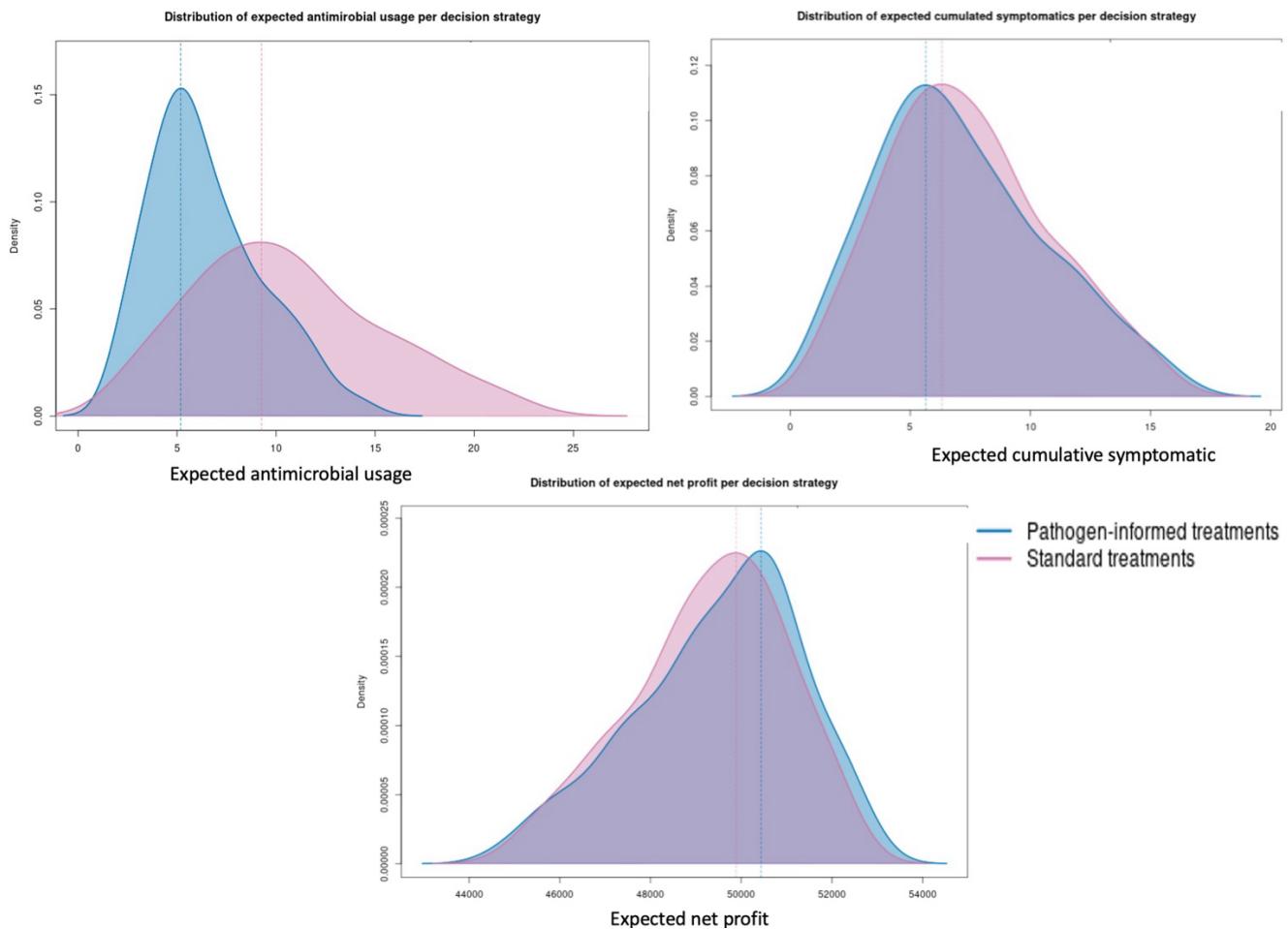
512 We next evaluated how the initial risk composition of a batch influences the accuracy of pathogen
 513 identification. [Figure 5.a](#) displays a ternary plot that maps balanced accuracy across varying
 514 proportions of low-, medium-, and high-risk individuals, revealing three distinct zones: high accuracy
 515 ($\geq 93\%$), moderate accuracy (88%–93%), and low accuracy (72%–78%). Batches dominated by high-
 516 risk individuals consistently achieved high accuracy, exceeding 93% in most cases. This suggests that
 517 the pronounced symptomatic trajectories in high-risk populations generate distinct outbreak
 518 dynamics, thereby facilitating more reliable pathogen differentiation. In contrast, batches with a
 519 higher proportion of low-risk individuals yielded lower classification accuracy, in some cases
 520 dropping to as low as 72%. The reduced severity and non-specificity of symptoms in these groups
 521 likely contribute to increased classification uncertainty.

522 When examining pathogen-specific performance [Figure 5 \(subplots b, c, d\)](#), BRSV maintained an
 523 accuracy above 96% in 57% of batch configurations and exceeded 80% in 95% of cases, particularly
 524 when high- and medium-risk individuals predominated. Conversely, the *Mh* model showed an
 525 accuracy range of 88% to 94% in about 37% of cases, with higher accuracies linked to batches with
 526 predominantly high-risk individuals; its performance declined in mixed or low-risk settings, reaching
 527 between 72% and 82% in 43% of cases. *Mb* was the most challenging to classify, with overall
 528 accuracy being the lowest among the three pathogens—10% of batch configurations exhibited
 529 accuracies below 72%—particularly in batches dominated by low-risk individuals where symptom
 530 trajectories overlapped more with those of BRSV and *Mh*.

531 Overall, a clear trend emerges: classification accuracy improves with an increasing proportion of high-
 532 risk individuals, while batches with predominantly low-risk calves are more prone to
 533 misclassification. This quantitative framework offers valuable insight into the epidemiological
 534 conditions under which BRD infectious agents can be most reliably identified, highlighting the critical
 535 influence of host risk heterogeneity on diagnostic performance.

537 3.2. Economic implications of pathogen-informed treatment decisions

538 3.2.1. Profitability assessment – Expected net profit



539
540 Fig 6: Pathogen informed treatment decisions versus conventional treatment decisions.
541
542

Table 6. Performance of pathogen informed treatment decision

Impact	Statistics	Conventional treatment decisions	Pathogen informed decisions
Expected net profit (K€)	Mode	49 886	50 432
	Std	1 697	1 816
Expected antimicrobial usage	Mode	9	5
	Std	4	3
Expected cumulative symptomatic	Mode	6	5.4
	Std	3	3

543
544 Results in this section present evaluation of the expected net profit of conventional treatment decisions
545 versus pathogen-informed treatment decisions (see 2.5.3 for detail).
546 The net profit is higher under pathogen-informed treatment than with conventional decisions (Figure

547 6), with a median value around 50,432 euros against 49,886 euros in the latter case – approximately
548 a 1% increase. Table 6 indicates that this approach also involves fewer antibiotic doses per batch,
549 with an average of five instead of nine (a reduction of roughly 44%), while the proportion of
550 clinically affected animals decreases marginally from to six to about 5.4 in average, a difference
551 that does not appear statistically significant (Mann-Whitney U test). The observed variability,
552 reflected in standard deviations approaching 1,800 euros for the net profit and around three to four
553 for antibiotic usage, confirms that this trend remains consistent across most simulated outbreak
554 scenarios.

555 The net profit under each strategy typically follows a moderately dispersed distribution (Figure 6),
556 with a central clustering around its respective median value and no strong skew visible in most. In
557 the pathogen-informed scenarios, the curve appears slightly widened, maybe suggesting a greater
558 variable financial outcome across different batch configurations. Regarding the antimicrobial usage,
559 the pathogen-informed curve is skewed to the lower end with a narrower distribution, suggesting a
560 consistent decrease in antimicrobial usage across different batch configurations.

561 562 4. Discussion

563 4.1. BRD infectious agent identification

564 Our theoretical investigation demonstrates that mechanistic models can effectively differentiate BRD
565 pathogens using early symptomatic data, achieving an overall classification accuracy of
566 approximately 93%. In particular, the BRSV model, with a true positive rate of 96%, clearly delineates
567 its outbreak signature from those of bacterial agents. From a modelling perspective, this high
568 performance could be a direct consequence of the properties of the discrete-time stochastic model
569 used, which rigorously captures the rapid transmission dynamics typical of airborne viruses. In
570 contrast, bacterial infections, especially those caused by *Mycoplasmopsis bovis*, present more gradual
571 and overlapping symptom patterns that result in slightly lower classification metrics. This nuance is
572 not merely an artifact of our modelling approach; it mirrors the real-world challenges faced by
573 veterinarians when diagnosing BRD, where subtle, chronic infections are notoriously difficult to
574 detect early. These outcomes are fully consistent with veterinarian knowledge; it is well established
575 that viruses like BRSV cause abrupt, pronounced clinical manifestations, whereas chronic bacterial
576 infections often yield subtler signs that complicate early diagnosis. This concordance between our
577 theoretical predictions and field observations is supported by recent studies. Moreover, the sensitivity
578 of our models to the initial risk composition of the herd - where higher proportions of high-risk
579 individuals enhance pathogen diagnostic clarity - is consistent with field data, reaffirming the critical
580 influence of batch composition on disease transmission.

581 One of the key benefits of this approach lies in its ability to distinguish cases likely caused solely by
582 BRSV from those involving bacterial pathogens. Such a distinction is crucial, as it opens the door to
583 more targeted treatment strategies, where antibiotics would not be used in cases where a viral infection
584 is strongly suspected. This advantage goes beyond economic considerations; it holds significant
585 public health implications by reducing unnecessary antibiotic consumption and mitigating the risk of
586 antimicrobial resistance.

587 However, it is important to acknowledge that these results are based on synthetic data, and although
588 the inherent stochastic variability enhances realism, validating our models against real outbreak data

589 is critical to assess their predictive reliability. Currently, there is no gold standard for evaluating
590 diseased animals based solely on visual appraisal of clinical signs, making ground truth determination
591 challenging. One promising direction for future research would be to explore how different thresholds
592 of diseased status influence the performance of pathogen identification through advanced model
593 selection methods. Optimizing the differentiation and identification accuracy of correct pathogens-
594 models (it is possible for veterinarians to biologically diagnose the nature of the infectious agents)
595 could thereby help veterinarians determine the optimal threshold of clinical signs for visual appraisal.

596 Furthermore, the mechanistic models employed in this study assume that a single pathogen dominates
597 throughout the outbreak, neglecting the possibility of co-infections or co-circulation. In reality,
598 multiple infectious agents often interact, with some pathogens acting as primary initiators and others
599 as secondary aggravators. As highlighted by Pinotti et al. (2019), such interactions can lead to non-
600 linear epidemiological patterns that complicate both diagnosis and disease management. Future
601 models should, therefore, incorporate co-infection dynamics. Extending our distinguishability method
602 to handle multi-label classification problems where an input signal may be attributed to multiple
603 pathogens with corresponding weights represents a natural and necessary progression to capture the
604 complexity of real-world outbreaks.

605 The blend of theoretical knowledge and empirical/practical veterinary knowledge could not only
606 enhance our understanding of BRD dynamics but also paves the way for developing reliable decision-
607 support tools that integrate epidemiological insights with practical treatment strategies.

608 609 4.2. *Expected profit from pathogen-tailored antibiotic treatments*

610 Results indicate that adopting a pathogen-informed decision process can provide a modest but
611 consistent financial advantage compared to conventional strategies. When using the early
612 symptomatic signals detected (5 days of observation) and mechanistic-model inference before
613 administering antibiotics, the median net profit reaches approximately 50,432 euros for a batch of 12
614 animals over the fattening period. By contrast, an empirical approach that treats all symptomatic
615 animals, irrespective of whether the pathogen is likely viral or bacterial, yields a slightly lower median
616 net profit of around 49,886 euros. Although this difference of about 546 euros represents only a
617 marginal increase of roughly one percent, the trend remains consistent across most simulated batch
618 configurations.

619 These findings also highlight a substantial decrease in antimicrobial usage, from an average of nine
620 doses per batch under the conventional protocol to about five doses under the pathogen-informed
621 strategy. This reduction, nearing forty-four percent, holds significance for both the stewardship of
622 antibiotic resources and the mitigation of antimicrobial resistance. In addition, the total number of
623 clinically affected animals across the fattening period decreases only slightly (from six to about 5.4),
624 and even though the difference in clinical outcomes does not appear statistically significant, these
625 simulations were realised with a single batch of 12 individuals, and the default probability of
626 recovering from an *Mannheimia haemolytica* infection is only 60%. Findings suggest that early,
627 model-based identification of bacterial versus viral aetiology can simultaneously preserve animal
628 welfare, improve financial benefit and substantially contribute to reducing the emergence of
629 antimicrobial resistance and save costs and time spent to buy and administer individual treatments.

630 Several limitations exist in our economic calculations. One key assumption is that all animals are

631 purchased at the same price, which does not always reflect real-world conditions. Additionally, the
632 model assumes simultaneous sale of all animals, disregarding the common practice of farmers
633 retaining those animals that have been adversely affected by disease. As such, our economic model is
634 not intended to be predictive in an absolute sense but rather serves as a framework for ranking
635 outcomes relative to each other to inform BRD control measures. Future research should aim to
636 incorporate more realistic assumptions, such as variable purchase and sale prices and dynamic
637 treatment protocols, to enhance the predictive power of the economic analysis.

638 Moreover, our study, which focuses on a single batch size of 12 animals, opens several avenues for
639 extension. In real-world settings, batch sizes vary considerably, and exploring scenarios with larger
640 or smaller populations could provide further insights into how group size influences both model
641 distinguishability and economic outcomes. Additionally, incorporating more effective or cheaper
642 control measures such as vaccination, isolation or metaphylaxis could offer a more comprehensive
643 assessment of the financial and welfare benefits, thereby refining the decision-making process for
644 BRD control.

645 Expected profitability fundamentally depends on the quality of treatment decisions taken. As
646 demonstrated by [J-S Pierre \(2023\)](#), the effectiveness of decision-making hinges not only on the
647 model's accuracy but also on the decision threshold used to determine the nature of the pathogen. In
648 our study, the decision threshold is defined as $M = \operatorname{argmax}_{m \in \mathcal{M}} P(M_i | S^*)$, meaning that the pathogen-
649 model with the highest posterior probability is the one recommended for decision-making. Exploring
650 how subtle shifts in this threshold affect profitability could reveal an optimal balance that maximizes
651 both pathogen identification and economic returns. Furthermore, our study raises the question of
652 whether a five-day observation window is optimal. Shortening this period might allow for earlier
653 interventions, but it could also compromise classification accuracy. Investigating this trade-off could
654 yield a more efficient protocol for early intervention, ensuring that initial classification translates into
655 robust long-term predictions of outbreak dynamics.

656 A key step toward building a more integrated and robust pipeline for real-world applications is the
657 explicit consideration of uncertainty. A common approach is to quantify prediction uncertainty
658 independently of its downstream impact on decision-making ([Yarin Gal et al., 2016](#); [J. Lampinen et](#)
659 [al., 2001](#); [E. Goan et al., 2018](#)). This can be achieved, for instance, by leveraging posterior
660 distributions in a Bayesian framework to construct uncertainty sets that uniformly encompass the true
661 outcomes across all predictions. The economic model can then select decisions that remain safe within
662 these uncertainty bounds. Such strategies have been successfully applied to provide safety assurances
663 ([Eyango et al., 2024](#)).

664 While our findings demonstrate the theoretical ability of mechanistic models to differentiate BRD
665 pathogens based on early symptomatic data, it is crucial to acknowledge that these results are derived
666 from simulated outbreaks. The inherent stochastic variability enhances realism, yet the models have
667 not been validated against real-world outbreak data. In practice, multiple pathogens often co-circulate,
668 and their interactions can complicate diagnosis and treatment strategies. Future research should focus
669 on empirical validation by testing these models against field data to refine their predictive power and
670 assess their robustness in real epidemiological conditions. Such validation would provide essential
671 insights into the applicability of these models as decision-support tools for veterinarians and farmers,
672 ensuring their relevance beyond controlled simulation environments.

673

674 **5. Conclusion**

675 Beyond its application to BRD, this work contributes to the broader methodological landscape of
676 model selection in epidemiology. Our approach exemplifies how to choose a statistical model that
677 aligns with real-world constraints while considering user impact. The potential application of this
678 framework extends beyond pathogen identification. Our methodology could inform the development
679 of decision-support tools that assists farmers in dynamically configuring their farm structures to
680 improve pathogen detection and/or economic efficiency. More broadly this framework provides a
681 generalizable approach for selecting the most appropriate epidemiological model based on user
682 constraints, economic considerations, and available observational data.

683 A key takeaway from this study is the importance of early decision-making. The earlier the
684 identification process is done, the sooner it can drive positive change by reducing antibiotic use,
685 improving animal welfare, and increasing economic returns (see [supplementary files](#) for results at
686 after 20 days). Given that our results demonstrate high accuracy in early pathogen identification, rapid
687 implementation is essential to maximize its impact. Furthermore, our findings suggest that our method
688 is not only efficient but also consistently outperforms empirical decision-making strategies. This
689 reinforces the idea that integrating model-based approaches into veterinary practice can elevate
690 diagnostic accuracy and enhance treatment effectiveness.

691

692

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700 **Authors' contributions**

701 Conception and design of the study: LE, SP, NP. Data acquisition and analysis: LE (simulation outputs
702 and analysis). Interpretation of data: ALL. Drafting of the manuscript: LE, HF. Revisions of the
703 manuscript: ALL. All authors read and approved the final manuscript.

704

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713 made for this study.

714

715 Availability of data and materials

716 Emulsion is an open-source software which can be installed as a Python module
717 (<https://sourcesup.renater.fr/www/emulsion-public>). The BRD pathogen-specific model file
718 (brd.yaml) is open-sourced and published in: <https://forgemia.inra.fr/dynamo/brd-models/brd-public>
719 in the branch “pathogen-specific-multibatch”.

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939

1 Supplementary information
2
3

4 **Table of Contents**

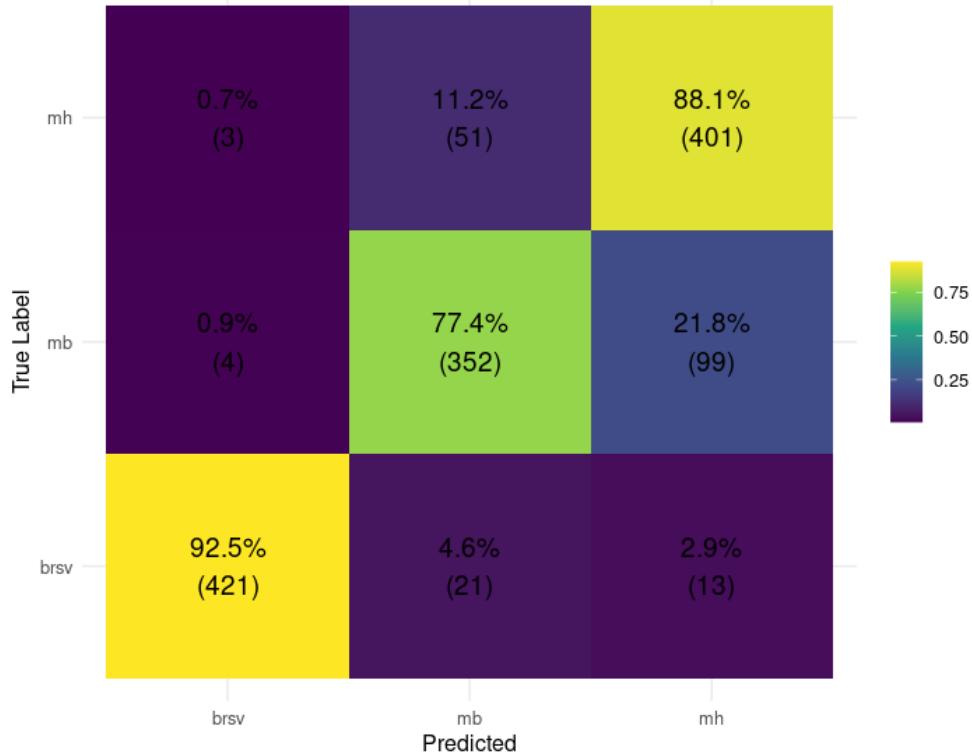
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10
11

12 **1. Model distinguishability – 20 days of observation**

13
14 This supplementary information provides quantitative assessments of the model distinguishability after 20 days
15 of observation of the detected symptomatic animals.

16
17 **1.1. Performance assessment of pathogen identification**



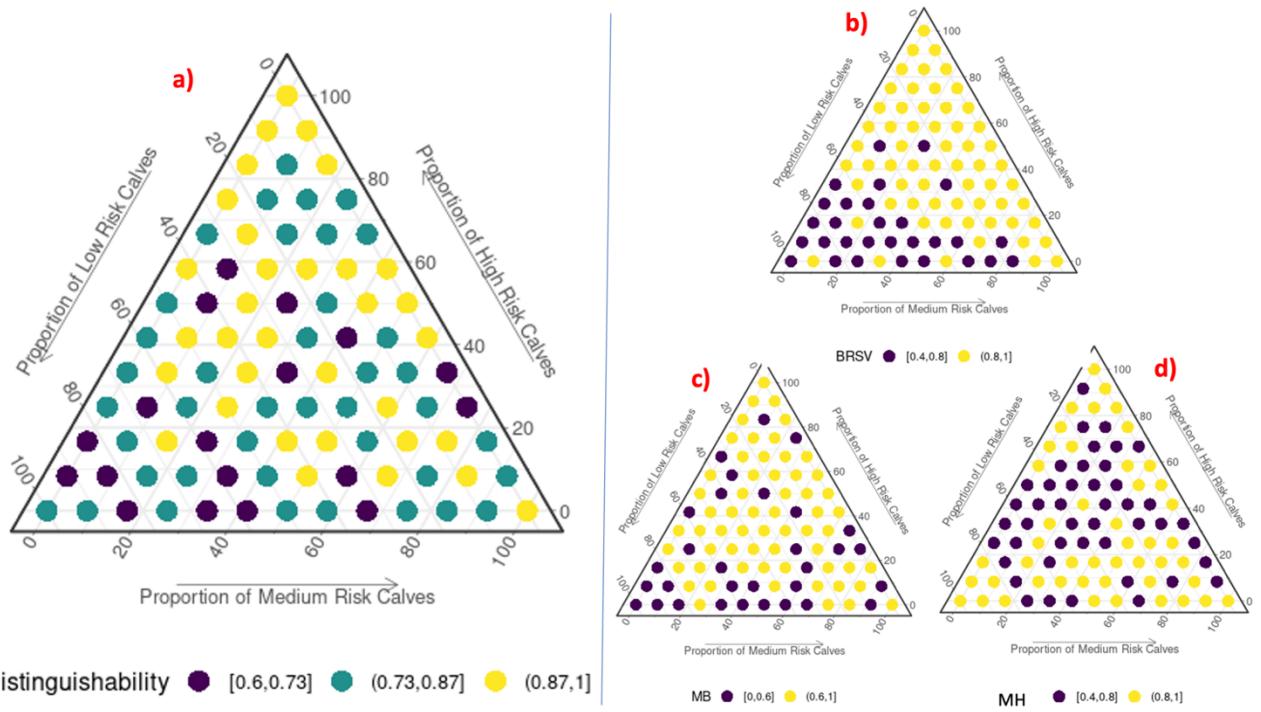
19
20 Figure 1: Confusion matrix. Classification performance for BRSV, MH and MB. The diagonal
21 represents correctly classified instance, while off-diagonal values indicate misclassifications
22 between classes.
23
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Table 1. Pathogens identifiability performances

Metrics	BRSV	MB	MH
True Positive Rate	0.9253	0.7736	0.8813
False Positive Rate	0.0077	0.0791	0.1231
Positive Predictive Value	0.9836	0.8302	0.7817
Negative Predictive Value	0.9637	0.8905	0.9366
Balanced Accuracy	0.99	0.95	0.96
Support	455	455	455

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31

1.2. Pathogen identification according to batch configuration

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33

34 Fig 02: Pathogen distinguishability map after 20 days of observing symptomatic dynamics. They represent
 35 the balanced accuracy of pathogen identification as a function of initial risk composition. The large ternary
 36 plot on the left is the overall classification accuracy. And on the right are the specific accuracies of each
 37 pathogen (one-vs-all approach)

38

2. Bioeconomic implications after 20 days of observation

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41 2.1. Profitability assessment

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45 2.2. Profitability according to batch configurations

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Chapter 4

A deep mechanistic model: Grounded mechanistic model for adaptive knowledge

4.1 Introduction

4.1.1 Contextual background

Modern sensor modalities (e.g., lung ultrasound, video and audio surveillance, etc) offer high-frequency, objective measurements that overcome many limitations of human observation (inter-observer variability, delayed reporting). However, these measurements represent only the observable manifestations of underlying pathophysiological processes and thus provide an incomplete, noisy “snapshot” of disease state—what Yoan Bourhis (2017) aptly describes as the “tip of the iceberg” .

Aleatoric uncertainty refers to the inherent noise and variability present in the data itself. In the context of sensor-based diagnostics—such as lung ultrasound videos of cattle, aleatoric uncertainty arises from factors beyond the model’s control: image acquisition artifacts, animal movement, inconsistent probe positioning, and intrinsic biological variability in disease presentation. Because aleatoric uncertainty reflects randomness in the observation process, it cannot be reduced simply by collecting more data; instead, it must be explicitly modelled so that downstream predictions correctly reflect the limits of information contained in each measurement. Epistemic uncertainty, by contrast, captures the model’s lack of knowledge about the correct mapping from inputs to outputs. This form of uncertainty is highest when the model encounters examples that are far from the distribution of its training data—rare clinical presentations, novel farm environments, or unforeseen sensor configurations. Unlike aleatoric uncertainty, epistemic uncertainty can be reduced through the acquisition of additional, representative training examples. Crucially, a model can output a high softmax score (traditional logits interpreted as probabilities) even when its epistemic uncertainty is large, leading to overconfident and potentially erroneous predictions [57].

Epidemiological forecasting relies on mechanistic models, which codify known biological relationships (transmission rates, immune response kinetics, within-host pathogen dynamics) into mathematically tractable systems of equations. While these models capture long-term disease trajectories and can simulate the effects of interventions at the population level, they are poorly informed by sensor data when observations are unstructured, sparse and noisy.

4.1.2 Article Originality and objectives

To what extent can automated short-term diagnostics derived from limited sensor observations effectively inform and specify a mechanistic epidemiological model for long-term disease prognosis? In this work, we propose and explore a novel hybrid methodology explicitly aimed at integrating deep learning, sensor-based diagnostics with a mechanistic epidemiological model (Fig 4.1). Specifically, we develop an approach that leverages short-term, sensor-derived diagnostics obtained from limited Lung Ultrasound (LUS) video data to inform parameter calibration in epidemiological models. We employ a Bayesian Deep Mechanistic approach to bridge sensor-based diagnostics and mechanistic forecasting. This integration aims to enhance the interpretability, and practical applicability of epidemiological prognosis, enabling accurate long-term disease management strategies from inherently limited and uncertain short-term observations.

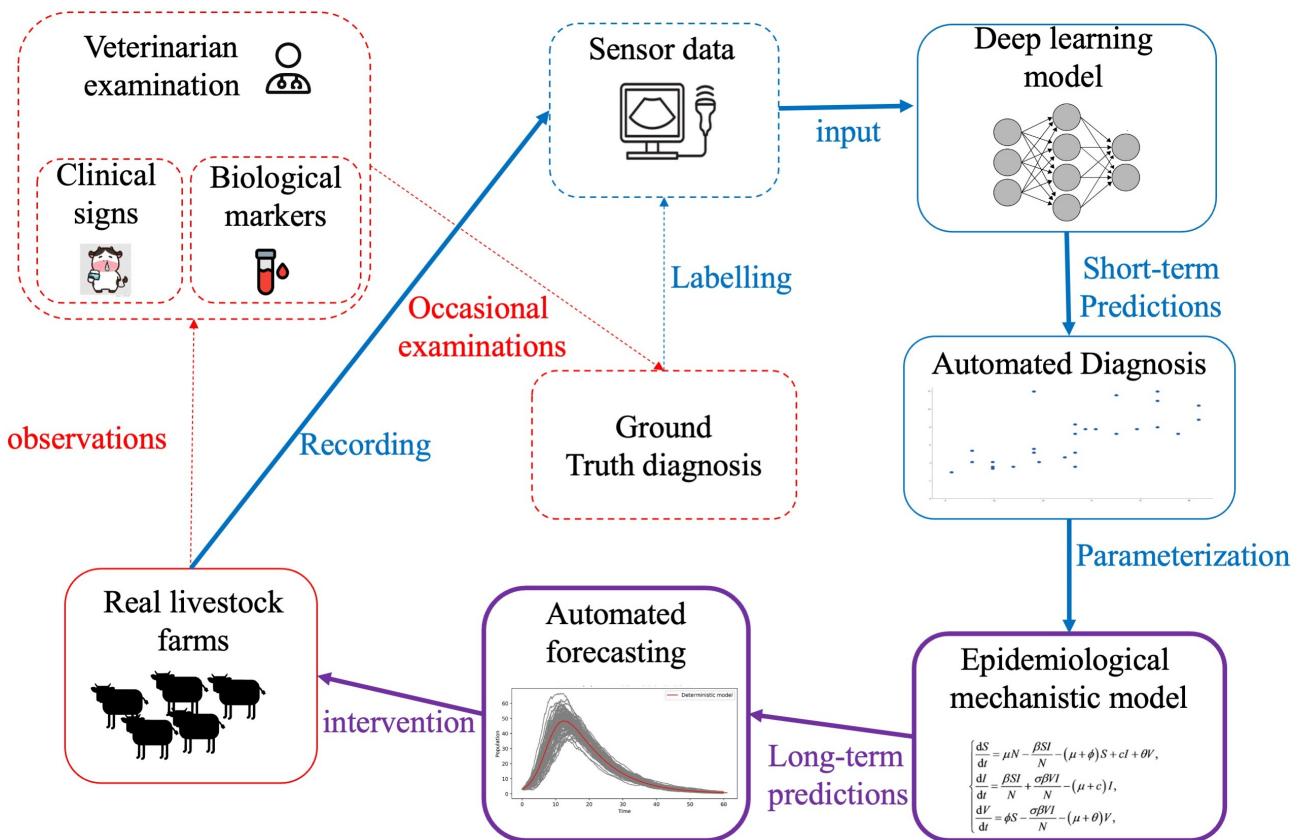


Figure 4.1: Sketch workflow of a ...

How can intrinsic uncertainties inherent in sensor-derived diagnostic data, especially noisy observations such as Lung Ultrasound (LUS) videos, be explicitly quantified and incorporated into mechanistic models to ensure a more robust and trustworthy prognostic prediction? Given the intrinsic uncertainty and noisiness of real-world LUS videos, exacerbated by animal movement and image acquisition limitations, this work explicitly addresses the quantification and integration of these uncertainties into the diagnostic and prognostic pipeline. We variational methods in Bayesian deep learning model to quantify the uncertainty associated with sensor-based diagnostic predictions. Bayesian probability theory offers us mathematically grounded tools to reason about model uncertainty. These quantified uncertainties are subsequently managed through two complementary approaches: either by filtering out high-uncertainty, unreliable observations (Out-of-distribution detection) to ensure safe prognosis and prioritize them for detailed veterinary reassessment, or by directly propagating uncertainties into mechanistic model calibration through

uncertainty-weighted parameter inference. This dual strategy enhances the robustness, reliability, and practical applicability of long-term prognostic predictions.

4.1.3 Main contributions

This chapter introduces the Bayesian Deep Mechanistic (BDM) model, a novel integrative approach that leverages both data-driven diagnostics derived from sensor technologies and knowledge-driven epidemiological modeling. This integration addresses critical limitations inherent in existing diagnostic and prognostic methodologies, specifically for Bovine Respiratory Disease (BRD), by explicitly quantifying and managing uncertainty from limited and noisy sensor observations. Three main contributions emerge from the approach presented in this chapter:

1. **Coupling punctual diagnostics with mechanistic forecasting (fig 4.2).** We designed and trained a hybrid deep learning pipeline, a spatio-temporal CNN-RNN—that ingests raw lung ultrasound (LUS) video clips and outputs a binary infectious status (infectious vs. non-infectious) for individual bovine. Our dataset comprised 265 LUS videos collected from 163 animals across nine French farms, capturing real-world variability in lesion appearance, probe positioning, and animal movement. Crucially, these “punctual” diagnostic predictions served not only as standalone classifiers but also as the empirical anchor for calibrating a mechanistic epidemiological model via Approximate Bayesian Computation (ABC). In practice, we treat each deep learning prediction as a point estimate of batch-level infection prevalence at discrete observation times; ABC then infers the three key parameters—initial prevalence, average infectious duration, and transmission rate—that best reconcile the mechanistic model’s simulated infection trajectories with these sensor-derived snapshots. This coupling bridges short-term, deep learning diagnostics and long-term, mechanistic forecasts.

Although fully automated and practical for on-farm use, our diagnostic model achieved a relative root-mean-square error (RRMSE) of 39% against veterinarian-confirmed labels, reflecting the inherent noise and variability of LUS data. When these predictions alone were used to parametrize the mechanistic model, the resulting 30-day forecast exhibited an RRMSE of 38.4%, substantially higher than the 23% error attained when using veterinarian ground-truth diagnostics. This gap underscores both the promise of automated sensing for scalable disease surveillance and the imperative of explicitly quantifying and managing uncertainty in order to approach the accuracy of expert-driven prognostics.

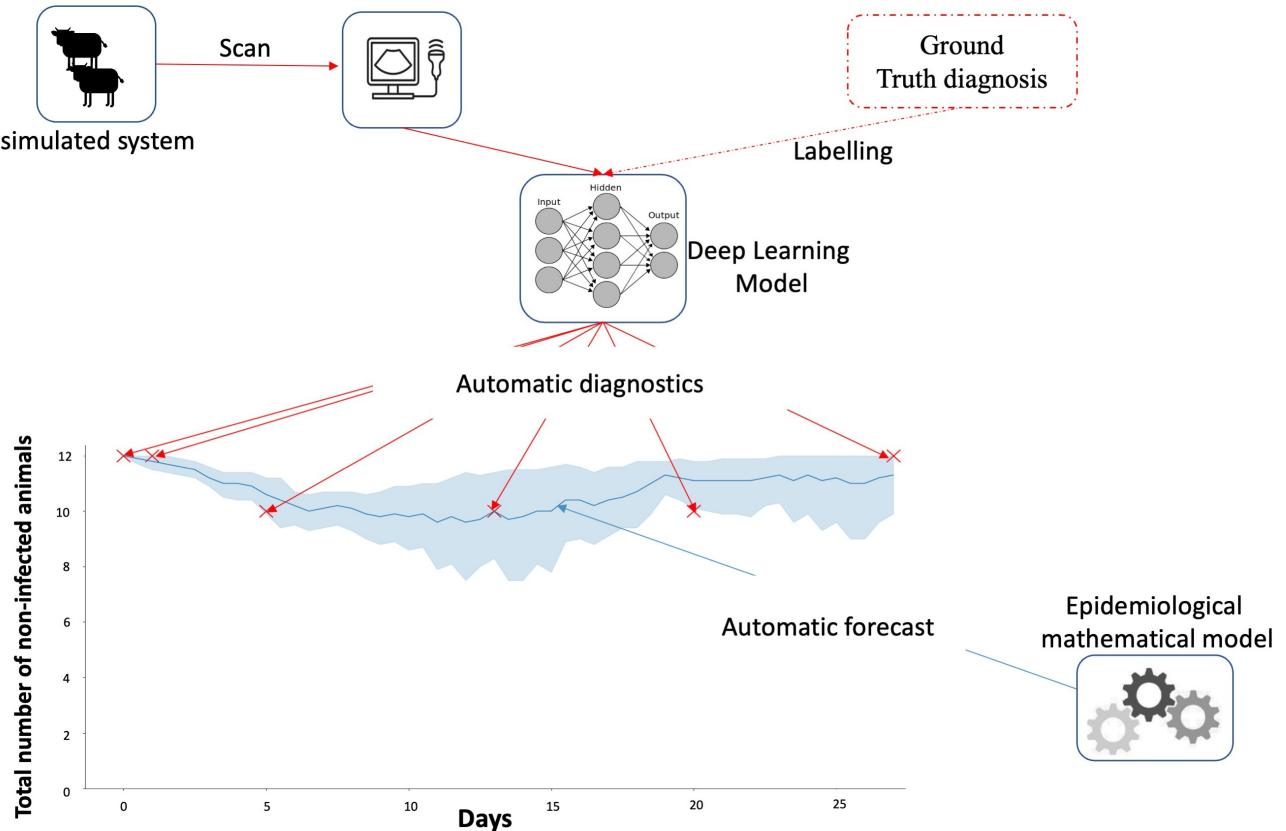


Figure 4.2: coupling punctual diagnostics with mechanistic forecasting

2. **Sensor observation cleansing through Uncertainty-Based Filtering (fig 4.3).** Lung ultrasound (LUS) videos are full with sources of noise, animal motion, suboptimal probe positioning, uninterpretable image artifacts—that can lead a deterministic classifier to make confidently wrong predictions (In chapter 1 2.2, we achieved only a 72% accuracy, for a binary classifier, that is low). In order to control this risk in observations used, we had to explicitly capture the epistemic uncertainty (i.e., the model’s lack of knowledge). For that we converted our CNN-RNN DL model into a Bayesian deep learning model using Monte Carlo Dropout (MCD). During inference, MCD performs dozens of stochastic forward passes with dropout active, producing a distribution of softmax probability vectors rather than a single point estimate. We then quantify uncertainty by computing the Shannon entropy of each video’s averaged class probability distribution—a well-established acquisition function in active learning that measures the spread (disorder) of predictive beliefs. High entropy indicates low confidence and signals inputs for which the model’s knowledge is insufficient.

By ranking predictions by entropy, we implemented an uncertainty-based filter: low-entropy (high-confidence) cases are accepted as automatic diagnoses, while high-entropy (low-confidence) cases are flagged for veterinarian review. This selective acceptance dramatically improved diagnostic accuracy, lowering the relative root-mean-square error (RRMSE) from 39% (deterministic predictions) to 32% against veterinarian ground truth. Crucially, when only filtered (high-confidence) diagnoses were used to calibrate our epidemiological model, the 30-day forecast error fell to 27.2% RRMSE—much closer to the 23% error achieved using full veterinarian diagnoses

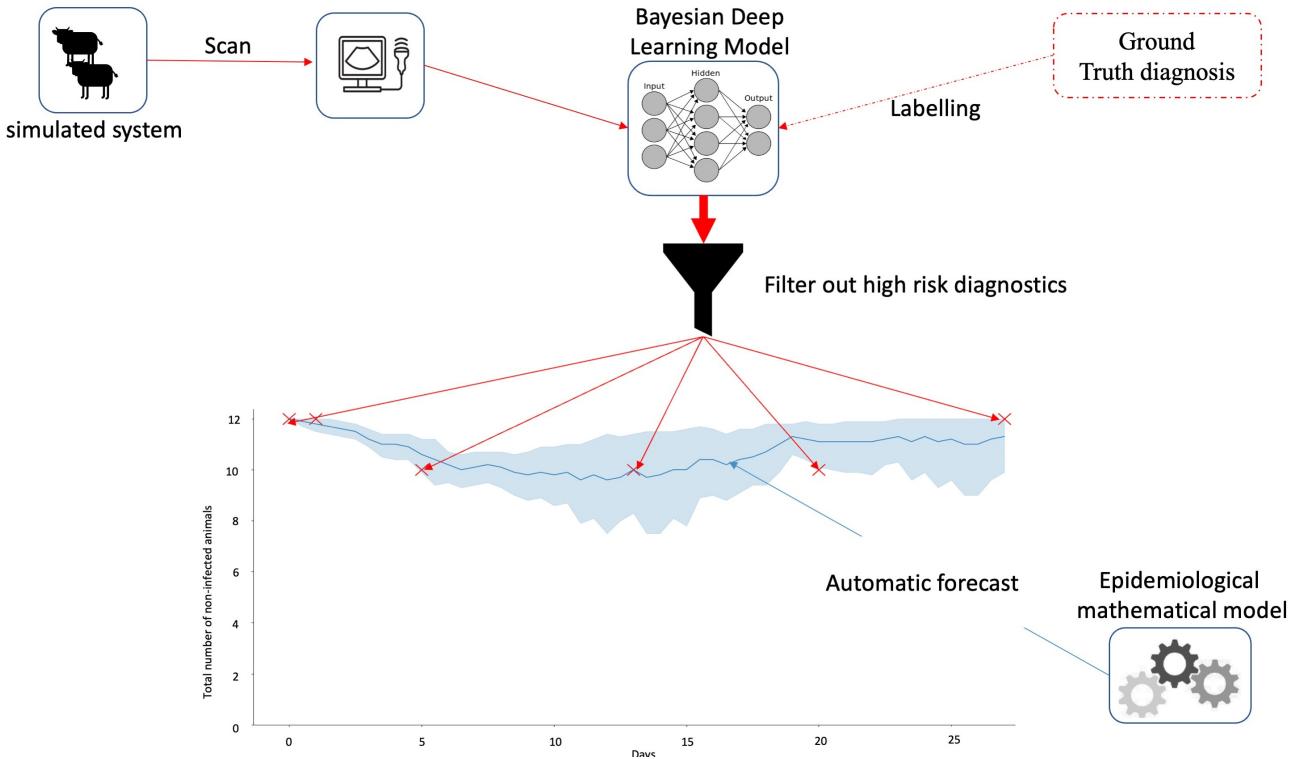


Figure 4.3: Sensor observation cleansing through Uncertainty-Based Filtering

3. **Prognosis robustness through Uncertainty Propagation (fig 4.4).** Rather than discarding low-confidence diagnoses, we leveraged each prediction’s quantified uncertainty to inform the parametrization of a stochastic mechanistic epidemiological model. After obtaining a posterior distribution (uncertainties) over batch-level infectious counts via Monte Carlo Dropout, we extracted both the mean (as the point estimate of infected prevalence) and its variance (as a measure of diagnostic confidence). During Approximate Bayesian Computation (ABC) parameter inference, we replaced the standard Euclidean distance with a weighted version in which each observation’s contribution was inversely proportional to its uncertainty (i.e., higher variance \rightarrow lower weight). This uncertainty-weighted inference ensures that reliable, low-variance diagnostics exert greater influence on parameter estimation (pathogen transmission rate, mean duration in the infectious state, mean duration in the pre-infectious state), while noisy, high-variance observations contribute less, effectively down-weighting potentially misleading observations rather than excluding it outright. The result is a more robust posterior over epidemiological parameters and, consequently, more accurate long-term forecasts: the uncertainty-propagated model achieved a 30-day forecast RRMSE of 27.2% nearly matching the 23% error obtained when calibrating solely on veterinarian-confirmed diagnoses. This method also reduces diagnostic error from the deterministic model’s 39% RRMSE to 32% RRMSE, matching the improvement seen in our uncertainty-filtering approach

These results demonstrate that explicitly propagating diagnostic uncertainty not only improves automated classification but also closes most of the remaining gap between sensor-based forecasts and expert-driven prognostics, unlocking robust long-term predictions from inherently noisy, limited observations. By embedding predictive uncertainty directly into the model calibration process, our approach preserves information from all sensor-based observations maximizing data utility, while mitigating the impact of noise.

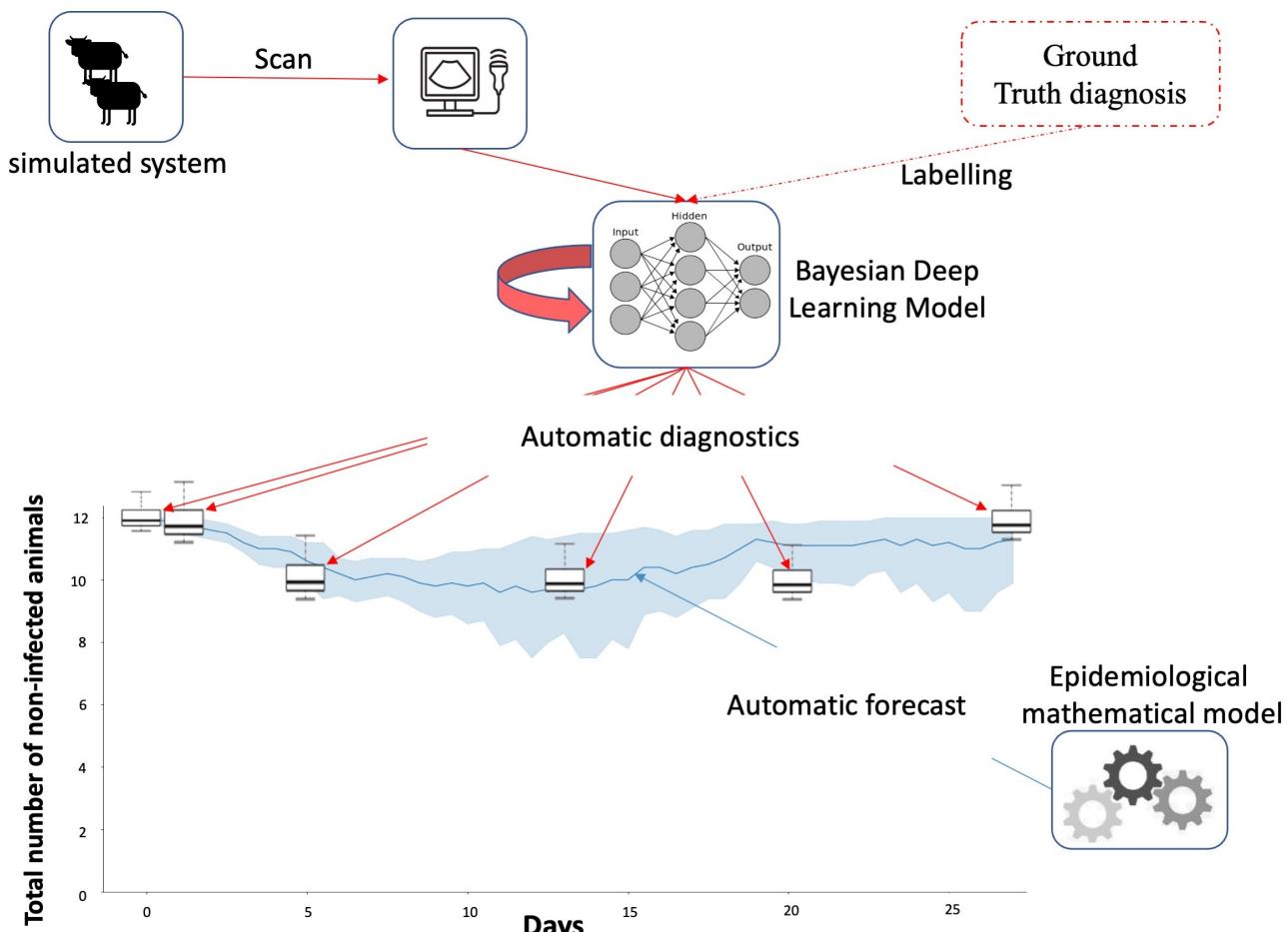


Figure 4.4: Prognosis robustness through Uncertainty Propagation

4.1.4 [In French] Résumé grand public

La santé animale et la prévention des maladies infectieuses reposent de plus en plus sur des technologies de diagnostic automatisées, comme l'échographie pulmonaire chez les bovins. Toutefois, ces données issues de capteurs sont souvent bruyantes, incomplètes et sujettes à des erreurs d'interprétation. Notre étude propose une nouvelle approche hybride qui combine l'intelligence artificielle (IA) et les modèles mathématiques traditionnels (appelés «mécanistiques») pour améliorer la détection précoce et la prévision à long terme de la maladie respiratoire bovine.

Nous avons d'abord développé un modèle d'apprentissage profond capable d'analyser automatiquement de courtes vidéos d'échographie pulmonaire et de prédire si un animal est infectieux ou non. Pour tenir compte de l'incertitude inhérente à ces diagnostics automatisés (problèmes de qualité d'image, mouvements de l'animal...), nous utilisons une technique bayésienne qui mesure la confiance de chaque prédition. Les cas où le modèle est peu sûr sont signalés pour un examen vétérinaire, soit pondérés de façon moindre dans les étapes suivantes.

Ensuite, ces diagnostics ponctuels, enrichis de leur degré de confiance, servent à calibrer un modèle épidémiologique mathématique qui simule la propagation de la maladie dans un troupeau sur plusieurs semaines. Cette intégration «fusion» permet de produire des prévisions de l'évolution de l'infection plus fiables que celles basées uniquement sur l'IA ou uniquement sur les modèles traditionnels. Concrètement, notre méthode réduit l'erreur de prédiction à 27% sur 30 jours – un résultat proche de la précision obtenue lorsqu'on utilise exclusivement des diagnostics vétérinaires, mais avec un processus entièrement automatisé et évolutif pour une utilisation directe en élevage.

En résumé, cette étude démontre qu'il est possible d'exploiter efficacement des données de capteurs imparfaites grâce à une modélisation hybride : l'intelligence artificielle apporte une analyse rapide et à grande échelle, tandis que le modèle mathématique garantit une prévision robuste à long terme. Cette approche ouvre la voie à une surveillance de la santé animale plus précise, proactive et accessible, contribuant à améliorer le bien-être des animaux et à réduire les pertes économiques liées aux maladies infectieuses.

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Harnessing uncertainty: A deep mechanistic approach for cautious diagnostic and forecast of Bovine Respiratory Disease

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ABSTRACT

Bovine Respiratory Disease (BRD) is a prevalent infectious disease of respiratory tract in cattle, presenting challenges in accurate diagnosis and forecasting due to the complex interactions of multiple risk factors. Common methods, including mathematical epidemiological models and data-driven approaches such as machine learning models, face limitations such as difficult parameter estimation or the need for data across all potential outcomes, which is challenging given the scarcity and noise in observing BRD processes. In response to these challenges, we introduce a novel approach known as the Bayesian Deep Mechanistic method. This method couples a data-driven model with a mathematical epidemiological model while accounting for uncertainties within the processes. By utilising 265 lung ultrasound videos as sensor data from 163 animals across 9 farms in France, we trained a Bayesian deep learning model to predict the infection status (infected or non-infected) of an entire batch of 12 animals, also providing associated confidence levels. These predictions, coupled with their confidence levels, were used to filter out highly uncertain diagnoses and diffuse uncertainties into the parameterisation of a mathematical epidemiological model to forecast the progression of infected animals. Our findings highlight that considering the confidence levels (or uncertainties) of predictions enhances both the diagnosis and forecasting of BRD. Uncertainty-aware diagnosis reduced errors to 32 %, outperforming traditional automatic diagnosis. Forecast relying on veterinarian diagnoses, considered the most confident, had a 23 % error, whilst forecast taking into account diagnosis uncertainties had a close 27.2 % error. Building upon uncertainty-awareness, our future research could explore integrating multiple types of sensor data, such as video surveillance, audio recordings, and environmental parameters, to provide a comprehensive evaluation of animal health, employing multi-modal methods for processing this diverse data.

1. Introduction

Bovine Respiratory Disease (BRD) is a prevalent, multi-factorial affliction impacting cattle worldwide, involving infections in both the upper and lower respiratory tracts (infectious bronchopneumonia), influenced by various causal agents (Smith et al., 2020). Cattle across all ages and production types, including dairy, beef, and veal, are susceptible. Although research has primarily focused on beef or feedlot calves (Edwards, 2010; Woolums et al., 2018), as well as dairy replacement heifers or veal calves, due to BRD's significance in these sectors (Dubrovsky et al., 2019; Pardon et al., 2013), it remains a critical

concern in all cattle populations. Untreated cases potentially leading to rapid performance decline and fatal pneumonia (Delabouglise et al., 2017; Engler et al., 2014). These statistics contribute significantly to economic losses, accounting for up to 20 % of farmers' annual incomes (Bareille et al., 2009). Diagnosing BRD is a complex and ambiguous process due to its potential interacting causes, including various pathogens such as bacteria and viruses, as well as non-infectious factors like the animal's genetics (breed, immunity, etc.) and environmental influences such as farming management practices (weaning, living conditions, treatments, etc.) (Gaudino et al., 2022; Murray et al., 2017). Antibiotics represent the primary treatment for BRD in the feeding

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period (Brault et al., 2019; Nickell and White, 2010), but their overuse raises concerns about the emergence of antibiotic resistance. Therefore, there is an urgent need to implement effective measures for studying the disease, controlling its spread, managing antibiotic usage and associated costs for farmers.

Various modelling approaches, encompassing data-driven methods such as machine learning algorithms, have been explored for diagnosing BRD. These algorithms, recognised for their effectiveness in applications like image recognition and natural language processing, have found multiple applications in veterinary research, predicting BRD (Cantor et al., 2022; Ramezani Gardaloud et al., 2022; Timsit et al., 2011). These methods extract BRD-related patterns by employing various sensors (ear-tag, intraruminal bolus, ultrasound scanner, etc) to record cattle behaviour, appearance and clinical signs. To minimise prediction errors, machine learning models adjust their internal parameters according to the given data. The performance and adaptability of these models heavily rely on the richness and diversity of collected data. However, the absence of a gold standard to diagnose BRD based on clinical signs (Timsit et al., 2016) makes early detection through sensor data alone susceptible to false alerts. Additionally, young beef cattle instinctively tend to conceal their clinical signs (Griffin, 2010), a behaviour that evolved as a survival tactic, further increasing the rarity of meaningful observations.

Unlike data-driven methods, knowledge-driven approaches, such as mechanistic models, are mathematical models designed to describe and represent the intricate relationships within a system. These models are constructed based on a set of rules derived from theoretical insights and empirical observations. In epidemiology, they find common application in predicting the dynamic behaviour of complex diseases like Covid (Plank et al., 2022), African swine fever (Muñoz et al., 2022), avian influenza (Lambert et al., 2023), and BRD (Picault et al., 2022). The primary strength of mechanistic models, in contrast to machine learning models, lies in their ability to simulate diverse scenarios without requiring extensive data. By simulating various disease management scenarios, such as surveillance, prevention, and intervention strategies, we can compare their effectiveness and offer evidence-based recommendations, guiding decision-makers to implement optimal control measures. Mechanistic models have demonstrated their efficiency for studying and controlling the spread of infectious diseases (Ezanno et al.,

2020). However, it is crucial to note that their calibration presents a substantial challenge. It is a tedious work to re-calibrate these models to specific real-world outcomes.

Our research aimed to devise an approach that adeptly addresses the constraints of both data-driven and knowledge-driven methodologies in epidemiology. We sought to develop a method capable of extracting insights from limited data sources while conserving its reliability in the face of noisy observations. More specifically, we crafted multiple scenarios to compare various methods of automatically extracting insights from sensor data using a data-driven model, and subsequently repurposing these insights to forecast the progression of BRD through a mathematical epidemiological model.

2. Materials and methods

The methodology of this work is structured as follows (Fig. 1): In the Section 2.1, we provide a detailed overview of the data acquisition process, encompassing pulmonary ultrasound videos employed as sensor data with the clinical and biological examination, established by veterinarians, serving as the ground truth to distinguish infected animals expressing clinical signs. In Section 2.2, a baseline scenario was devised, where veterinarian expertise was used to reliably diagnose the total number of infected animals at several observation dates over a 30-day period. Crucial epidemiological parameters of a BRD mechanistic model were then inferred enabling the forecast of the optimal path of the evolution of the total number of infected animals. In subsequent sections, 2.3, 2.4, 2.5), we devise multiple methods to automatically estimate the total number of infected animals, to improve the diagnostics and forecast by incorporating uncertainty-based approaches to filter out noisy observations or propagate the uncertainty of the diagnostics to the forecasting. To conclude, the diagnostic and forecast performance of each method is assessed in comparison with the baseline scenario 2.2.

In our study, we use the term "diagnosis" to refer to predictions made instantaneously based on current data. In contrast, we use 'forecast' to describe the prediction of future disease progression, utilizing current diagnostic data to project outcomes over time.

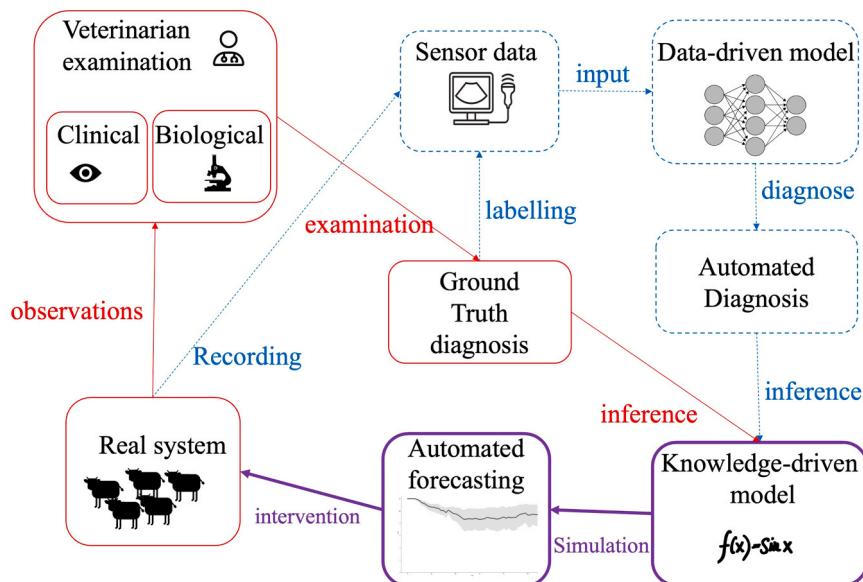


Fig. 1. Workflow of Bayesian deep mechanistic model. A real system is a farm containing animals in batches. Red path: Traditional approach involving manual diagnosis from veterinarian examinations, employed for parameter inference of a knowledge-driven forecast. Blue path: Integration of lung ultrasound sensor for automated data collection labelled with veterinarian-established ground truth, followed by a data-driven model trained to automate the diagnoses which are re-used along with their confidence levels in several ways to improve and automate the forecast through a knowledge-driven model enabling tailored interventions.

2.1. Data acquisition process

The data used in the experiments were gathered from nine fattening farms in western France. Each farm managed up to three batches simultaneously, with each batch consisting of an average of five to twelve calves. Of the total cattle, 78 % of Charolais breed, 12 % of Limousin, and 10 % mixed breeds. The Charolais breed was predominantly chosen because it is among the most prevalent beef breeds raised in France. The experimentation on each farm started on the day the cattle arrived (Day 0), for a duration of one month. The initial weeks following their arrival are considered the period when cattle are most susceptible to BRD (Babcock et al., 2009). Consequently, the data collection period spanned from January to June 2023. To simplify readability of the paper, let's denote by $t \in \{1, 5, 14, 21, 28\}$ the observation dates. The selection of examination dates varied among farms and depended on the availability of both farmers and a veterinarian.

2.1.1. Sensor data

Portable ultrasound scanners were employed to evaluate the animals' lung conditions on multiple days $t \in \{1, 5, 14, 21, 28\}$. The ultrasound scanner captured lung images in video format, featuring 28 frames per second in black and white, lasting up to 20 seconds each, with a resolution of 480×560 pixels. The animals' lungs were partitioned into eight inter-costal zones, following a standardised scanning protocol from the shoulder to the stomach: Ultrasound scanning was conducted on the 4th and 5th intercostal spaces. These spaces are the most cranial intercostal spaces accessible in animals of this size and age, as referenced by (Cuevas-Gómez et al., 2020). Each intercostal space was further divided into ventral and caudal portions, separated by the shoulder, resulting in four sections scanned per side for each animal. A veterinarian validated the dataset and, in some farms, ultrasound was only performed on one side of the animal because of the physical restraints we encountered. Within the local farming system, it was challenging to establish a recruitment criterion that mandated access to both sides of the thorax, alongside other criteria such as internet access and a sufficient number of animals purchased annually. The process of recording videos with an ultrasound scanner proved to be time-consuming, tedious, and challenging, requiring the animals to be kept in a fixed position. Consequently, some animals were prioritised for the study, only the ones having lesions larger than 1 cm^2 were deemed meaningful (Masset et al., 2022). If multiple significant lesions ($> 1 \text{ cm}^2$) were observed in the same intercostal area, only one video was recorded, corresponding to the lesion with the largest surface area. On Day 0 ($t = 0$), one-third of the animals of the three batches underwent examination, while from Day 2 to Day 28 ($t > 0$), all animals in a selected batch were examined. To maintain a balanced dataset, videos of clinically healthy lungs, without lesions, were also recorded. To simplify further explanation, we denote by $\mathcal{X}^{\text{obs}} = \{x_1^{\text{obs}}, x_2^{\text{obs}}, \dots, x_i^{\text{obs}}, \dots, x_n^{\text{obs}}\}$ the space containing the Lung UltraSound (LUS) video $x_{n,t}^{\text{obs}}$ for each individual i at time t . Note here that at a given time t , an animal having lesion (so scanned) in a given batch may vary since some lesion may disappear over time.

2.1.2. Ground truth data

Ground truth data consists in the identification of diseased animals, based on clinical and biological assessments. Multiple veterinarians participated in the examination of the animals, having undergone identical training to minimise annotation bias. Clinical assessments involved the examination of rectal temperature, lethargy, nasal/ocular discharge, and quantification of breathing rate/amplitude. Animals were categorised as clinically diseased if their rectal temperature exceeded 39.7°C (Timsit et al., 2011) and if they had at least one more clinical symptom, which helped to reduce false positives caused by non-infectious events. Biological assessments involved the use of nasal

swabs to determine the presence or absence of BRD associated pathogens (*Mannheimia haemolytica*, *Pasteurella multocida*, *Mycoplasma bovis*, *Histophilus somni*, Bovine Respiratory Syncytial Virus, Para-influenza Virus type 3, bovine coronavirus, Influenza D virus). This choice was primarily made due to restraint issues, the duration of the procedure, and the invasiveness of the alternative methods. Following collection, the swabs were immediately placed on ice and transported to the laboratory within three hours. There, the two swabs from each animal were suspended in 400–600 μL of phosphate-buffered saline (PBS) and stored at -80°C . PCR analyses were performed within a maximum of 6 months from freezing at the BIOEPAR laboratory (UMR BIOEPAR, France), using a range of commercial kits (BIOTK051, BIOTK052, BIOTK053, BIOTK054, Biosellal, France). An animal was considered biologically diseased if it had at least one of those pathogens. The final decision of whether an animal was considered infected or not was made using a combination of clinical and biological results (see Table 1). Clinical signs of BRD are often observed late in the disease course (Schaefer et al., 2007), this is partly caused by the fact that sick animals tend to hide their clinical signs. Therefore, in this study, we hypothesised that biological exams provide more informative insights than clinical exams. Consequently, when there was a disagreement between the two types of exams, the biological exam was considered the final decision. To simplify further explanation lets denote by $\mathcal{Y}^{\text{obs}} = \{y_1^{\text{obs}}, y_2^{\text{obs}}, \dots, y_i^{\text{obs}}\}$ the space containing the infection

state $y_{i,t}^{\text{obs}} \in \{\text{Infected}, \text{non-infected}\}$ for each individual i at $t \in \{1, 5, 14, 21, 28\}$

Table 1 describes the data used for this study and Fig. 2 illustrated how we went from 5 to 12 animal per farm to 1254 individuals in total. In total, our study involved 9 farms, with each farm hosting up to 3 batches simultaneously. Each batch typically consisted of 5–12 animals. Veterinarians examined these animals over approximately 30 days, with multiple observation dates (e.g., $t=1, 5, 14$, etc.). We treated each observation of an animal as a distinct statistical individual. Although we initially had 12 unique animals, the total number of observations (and thus statistical individuals) increased to 1254. They were a total of 202 different bulls in the 1254 observations, the median number of observations per bull is 1 and the interquartile range is 4. It is important to clarify that these 1254 observations do not represent unique animals, as some were observed multiple times on different dates. A total of 1254 individual data points clustered in individual animals \mathcal{Y}^{obs} were examined by veterinarians to determine their infection state \mathcal{Y}^{obs} . Note that, only a subset of individuals in \mathcal{Y}^{obs} were recorded for LUS videos, specifically 163 individuals. And since each individual can be scanned on different zones (depending on the zones containing lesions), the total number of recorded LUS video \mathcal{X}^{obs} amounts to 265. Each recorded LUS video in \mathcal{X}^{obs} is associated to a unique infection state in \mathcal{Y}^{obs} such that we have 265 independent pairs $(x_1^{\text{obs}}, y_1^{\text{obs}}), \dots, (x_{265}^{\text{obs}}, y_{265}^{\text{obs}})$. This also means that 1091 individuals (87 %) in \mathcal{Y}^{obs} did not have a recorded LUS video in \mathcal{X}^{obs} .

2.2. Baseline scenario

2.2.1. BRD mechanistic model

In this study, we employed a well-established epidemiological mathematical model (Fig. 3) for BRD developed by (Picault et al., 2019a). This model is a stochastic individual-based mechanistic approach and had been initially calibrated (Picault et al., 2022) to investigate the influence of farming practices, particularly pen size and associated risk levels, on the dynamics of BRD, including its morbidity, severity, lethality, and antimicrobial usage. Their results highlighted the significant impact of risk reduction strategies implemented during pen formation, as well as the effectiveness of collective treatments in mitigating BRD incidence within high-risk pens.

Implementation and simulation of BRD mechanistic model was

Table 1

Infection State assignment guidelines. Observations can either be clinical or biological. Decision of infection state of an animal is based on the combination of observations. Quantities are subdivided into 3 categories.

Observations		Decision	Quantities		
Clinically diseased	Biologically diseased	Infection state (δ_i^{obs})	No. of observations examined ¹	No. of observations scanned ²	No. of LUS video recorded ³ (\mathcal{X}^{obs})
Yes	Yes	Infected	68	15	31
Yes	No	Non-infected	15	2	2
No	Yes	Infected	128	9	19
No	No	Non-infected	30	4	6
NE*	Yes	Infected	0	0	0
NE*	No	Non-infected	0	0	0
Yes	NE*	Infected	93	15	29
No	NE*	Non-infected	910	118	178
NE*	NE*	Undefined	10	0	0

¹ Total number of animals examined by veterinarians

² Total number of animals having gotten scanned for LUS

³ Total number of LUS Videos recorded

* (NE) Not Examined animals

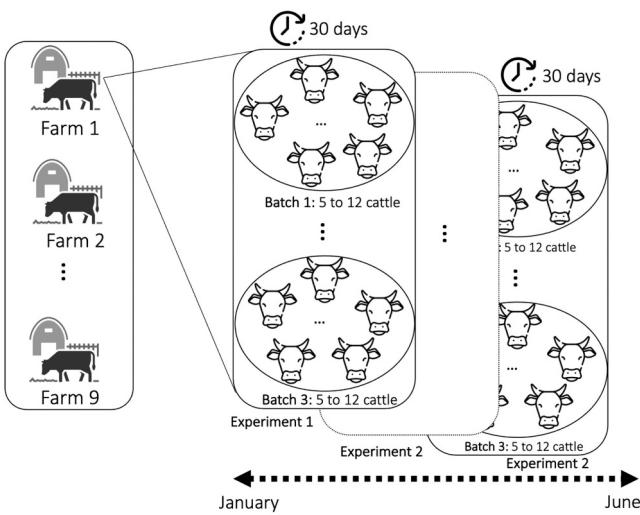


Fig. 2. Total number of individuals. Going from farm having 5–12 animals, we end up with over 1000 individuals if we consider each individual to be independent at each observation date.

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.

2.2.2. Model calibration

The reliability and realistic performance of a mechanistic model depends on the behaviour of its internal parameters. Parameter inference refers to optimally adjusting the values of its parameters such that the mechanistic model can accurately represent real-world observations. In other words, inference fine-tunes these parameters, aligning the BRD mechanistic predictions closely with actual veterinarian diagnosis. The sensitivity analysis (Table 2) in (Picault et al., 2022), aiming to

Table 2

Definition of the three parameters of the BRD mechanistic model to be estimated.

Parameter definition	Notation	Min	Default	max
Initial Condition				
Initial Prevalence (No units)	θ_1	0.0	0.1	1.0
Epidemiological parameters				
Average duration in Infectious State (hours)	θ_2	0.0	120	+ inf
Pathogen transmission rate (h^{-1})	θ_3	0.0	0.008	1.0

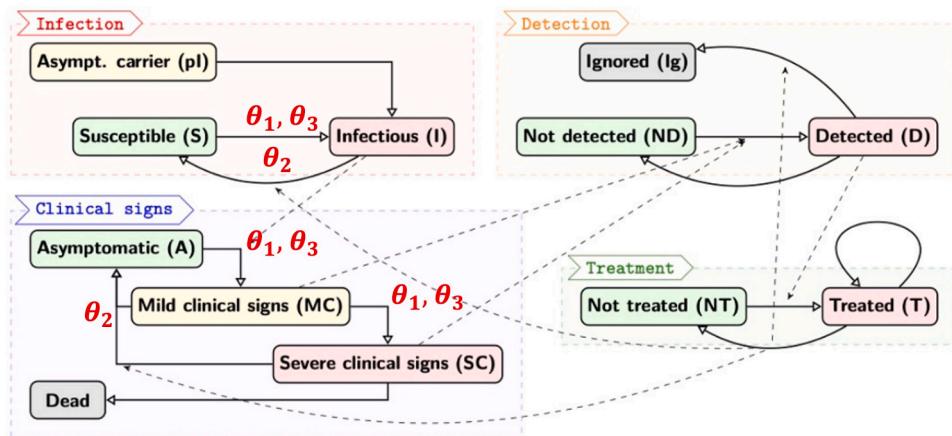


Fig. 3. Overview of the process's representation in the mechanistic BRD model (Picault et al., 2022). It integrates four processes (infection, clinical signs, detection, treatment). Animals transitioning to the infectious state (I) also exhibited mild clinical signs (MC), which can be detected (D), leading to initial treatment (T) that can be repeated. Successful treatment causes the animal to revert to susceptible (S) and asymptomatic (A) states. If successive treatments failed, the process will stop, and the animal will be 'Ignored' (Ig).

understand the importance of each parameter in the final prediction, emphasised the significance of parameters like the pathogen transmission rate and the average duration in the infectious state, critical for managing antimicrobial usage and mortality rates. In the present study, we focused on determining the optimal values of three crucial parameters, $\theta_1, \theta_2, \theta_3$ as described below.

Table 2 outlines the meaning and permissible range of each parameter. The default values for these parameters are derived from the original publication of the mechanistic model by Sébastien Picault (Picault et al., 2019a): Initial Prevalence represents the initial proportion of infectious animals within the batch. Average Duration in Infectious State indicates the average time an animal remains in the infectious state. Pathogen Transmission Rate reflects the average rate at which a pathogen is transmitted from one animal to another. To estimate these parameters, we employed a likelihood-free inference method called Approximate Bayesian Computation (ABC) (Beaumont, 2019), specifically regression-based correction methods. This method entailed sampling randomly, in this particular case 100, parameter values within a biologically acceptable domain and utilising them to generate simulated datasets through the "average" pathogen model. Selected summary statistics, specifically, here the count of symptomatic animals, captured essential features of the observed data and related predictions of the deep learning model. The similarity between simulated and observed data was assessed using the Euclidean distance, and the top 1% of sampled parameters were accepted. This process facilitated the estimation of the distribution of potential values for the selected parameters. A type of regression-based ABC method, ABC-NN (i.e., regression by neural network), was chosen.

It's noteworthy that the Euclidean distance, with equal weights assigned to every point, was used as the distance measure to compare observed and simulated data. This implies an assumption that all observations were made with the same confidence level.

2.2.3. Baseline implementation

In conclusion of this section, we created a scenario **Fig. 4**. Ground truth data (**Table 1**) is used to determine the infection status of each animal $y^{obs} \in \{\text{Infected}, \text{non-infected}\}$. By aggregating these results, we obtained the total counts of infected and non-infected animals over time, we refer to this information as diagnostics (**Fig. 1**). Similarly, since the mechanistic model (**Fig. 3**) can predict the numbers of infectious (I), susceptible (S), and asymptomatic carriers (pi), if we express the

model's output as non-infectious being the sum of Susceptible Asymptomatic Carriers, then we can obtain the total counts of infected and non-infected animals over time, we refer to this information as forecasting (**Fig. 1**). Diagnostics are made during veterinarians' visits (once per week on average) whereas forecasting allows a continuous monitoring of the total number of infected animals because its predictions are computed more often (every 12 hours). The ABC parameter inference is employed to estimate the optimal values of the three crucial parameters of the BRD mechanistic model such that its forecasting path can pass closest to the veterinarian diagnostics. This way we can better study the evolution of the disease. In theory, since the mechanistic model follows a set biological rule, its predictions could help inform future diagnostics of veterinarians. This scenario serves as our baseline, against which the diagnostic and forecast performance of subsequent methods presented in this paper will be discussed.

2.3. Automatic diagnostics from a punctual estimator

2.3.1. Deep learning

The baseline method outlined in the previous section is a classical approach used by modellers to construct and estimate the parameters of epidemiological models using real-world observations. This approach relies on veterinarians' diagnostics, necessitating clinical and biological examination of every animal during each visit. This implies that a farmer would have to schedule a veterinarian visit, round up all the animals, individually consult each one—a process that is laborious, tedious, costly and susceptible to human errors. Given the many obstacles to regular diagnosis, we propose in this section an approach aimed at automating the diagnosis. We developed in this section a spatiotemporal convolutional neural network (deep learning model) to predict the infection state $y_i^{obs} \in \{\text{Infected}, \text{non-infected}\}$ of individual animals using their LUS videos x_n^{obs} as input.

The processing of the input dataset \mathcal{X}^{obs} (LUS videos) followed several steps. Initially, we addressed data imbalance in our LUS video database. Out of the 163 individuals recorded (**Table 1**), 24% were diagnosed as infected animals by the veterinarians, and the remaining 76% were non-infected animals. To create a balanced dataset, we applied a downsampling strategy to reduce the total number of non-infected individuals in the database. However, even with an equal number of individuals in each class, 70% of LUS videos belonged to non-

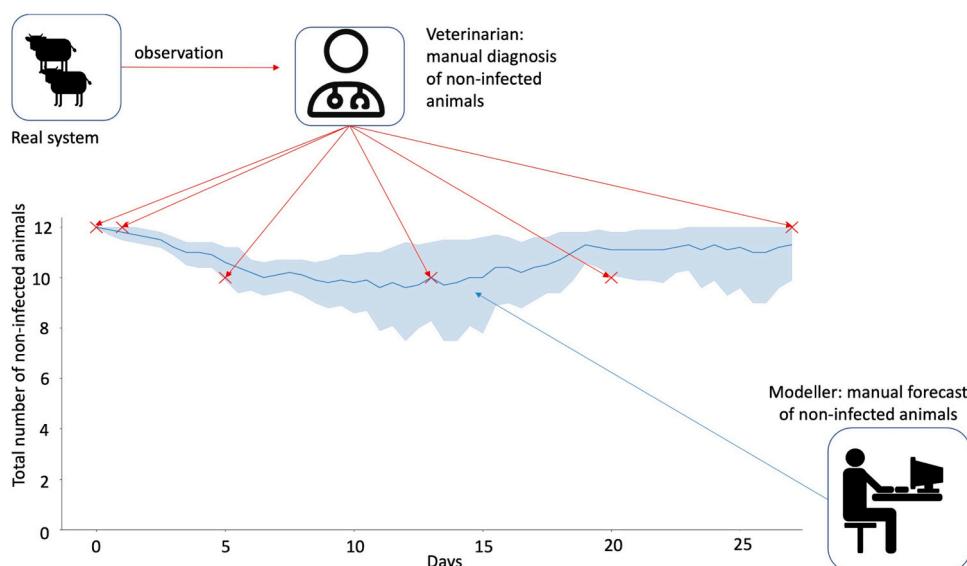


Fig. 4. Baseline Scenario: Traditional BRD study method - Veterinarians diagnose at different time steps animal infection states based on clinical and biological observations. Using these diagnoses, a modeller employs ABC inference to parameterise an average pathogen BRD mechanistic model (via Emulsion). This model enables the forecast of the total number of non-infected animals over a 30-day period.

infected animals due to some animals being scanned multiple times in different zones (see Sensor Data). Consequently, a second downsampling strategy was applied to reduce the number of LUS videos in the non-infected category. In the second step, the data obtained in the first step was split into a training set (comprising 70 % of videos), a validation set (comprising 20 % of videos), and a test set (comprising 10 % of videos). We ensured data integrity by preventing different videos of the same individual on the same day from appearing simultaneously in

however that is not the case here. To solve this issue, we had to artificially re-create a scenario where each examined individual has at least one corresponding LUS video. **Algorithm 1** illustrates how a bootstrap sampling algorithm was used to generate a LUS video set x_n^{sim} for each examined individual over time. This enables us to create a proper set as input for an automated pipeline such as the one presented in this work.

Algorithm 1. Population simulation through bootstrap sampling

Input : a scalar of the observed animals over time y_n^{obs}
Output: a scalar of the simulated LUS x_n^{sim}

- 1 **Initialisation;**
- 2 Create sampling pool of LUS video \mathcal{A} ;
- 3 **Re-sampling Process;**
- 4 **for** each Time Step (Examination Day) **do**
- 5 **for** each animal examined y_i^{obs} in y^{obs} **do**
- 6 Select randomly (with repetition) a LUS video from A such that
 $x^{sim} \leftarrow \pi(A);$
- 7 **end**
- 8 **end**

different sets, thus avoiding data leakage. For the test set, we used the complete data from the two farms that were set aside earlier when building the baseline method. In other words, the test dataset is both used to evaluated the performance of the deep learning model (automatic diagnostics) and mechanistic model (forecasting). Handling ultrasound videos posed challenges due to varying frame counts (technical issues when recording) and noisy images (moving animals). The solution employed, similar to handling text sequences, involved extracting images from the videos up to a maximum count and if a video had fewer images, the missing frames would be padded with zeros (Birnbaum et al., 2019).

A video encompasses both spatial information within individual frames and temporal information across the entire sequence. To effectively address both aspects in video analysis, we opted for a hybrid architecture, specifically a spatiotemporal convolutional neural network. In our approach, we integrated convolutional layers (Krizhevsky et al., 2017) with recurrent layers (Bengio et al., 1994). The convolutional layers focus on extracting spatial features, such as lesions, pleura lines, or other relevant anatomical details, while the recurrent layers capture temporal information related to the sequence or frequency of appearance of spatial features. For additional details about the architectures, including the chosen backbone, the number of layers, etc.

The code for implementation is written in Python (Version 3.8), utilising Tensorflow (Version 2.15.0) and Keras (Version 3.0.0) libraries to build, train, and evaluate the deep learning architecture. Optimisation was performed to find the best hyper-parameters using the Keras-Tuner library (Version 1.4.6). Additionally, experiment tracking was employed to monitor trained models through the use of the MLflow library (2.10.2).

2.3.2. Scenario simulation

Out of the nine farms, we set aside the data from two farms (testing set presented earlier), creating a sampling pool \mathcal{A} of LUS videos x_i^{obs} . In a perfect world every examined individual $y_n^{obs} \in \{\text{Infected}, \text{non-infected}\}$ in those two farms should have been recorded for LUS video x_n^{obs} ,

Out of the 9 farms 5 (Fig. 5), data from 2 farms were set aside specifically to evaluate the performance of the deep learning model, while the remaining 7 farms' data were used for training. To address the issue of missing data (38 videos), the test sample was reused as a sampling pool, allowing us to create a complete dataset. This sampling pool was ultimately used to assess the performance of the method we developed. The baseline accuracy represents the optimal outcome given that diagnoses are made by veterinarians and forecasts are based on their predictions. Therefore, our goal is to achieve an accuracy as close to this baseline as possible.

2.3.3. Method 1

In contrast to the baseline scenario where veterinarians manually provided diagnostics, in the current scenario, we trained a deep learning model to automatically diagnose $y_i^{obs} \in \{\text{Infected}, \text{non-infected}\}$ all individuals using only their LUS video x_i^{obs} (Fig. 6). In other words, we replaced the veterinarian diagnostics in Fig. 1 with predicted diagnostics. The subsequent steps mirrored the baseline approach, utilising ABC-NN to calibrate a BRD mechanistic model for optimal alignment with the predicted diagnosis. Regarding the diagnostics, it is important to note that we had to assign a virtual LUS video x_i^{sim} to every individual y_i^{obs} since they were not all scanned (as presented in the previous subsection "scenario simulation"). The evaluation of method 1 involves three steps: first, we compared its diagnostics performance with that of the baseline using the Relative Root Mean Square Error (RRMSE).

$$\text{RRMSE}(y_i^{\text{diag,pred}}, y_i^{\text{diag,obs}}) = \sqrt{\frac{\frac{1}{n} \sum_{i=1}^n (y_i^{\text{diag,pred}} - y_i^{\text{diag,obs}})^2}{\sum_{i=1}^n y_i^{\text{diag,obs}}} * 100}$$

Secondly, we assessed its forecasting performance relative to the baseline by employing the same metric, RRMSE. Finally, we compared the posterior distribution of parameters obtained using method 1 with that obtained under the baseline scenario.

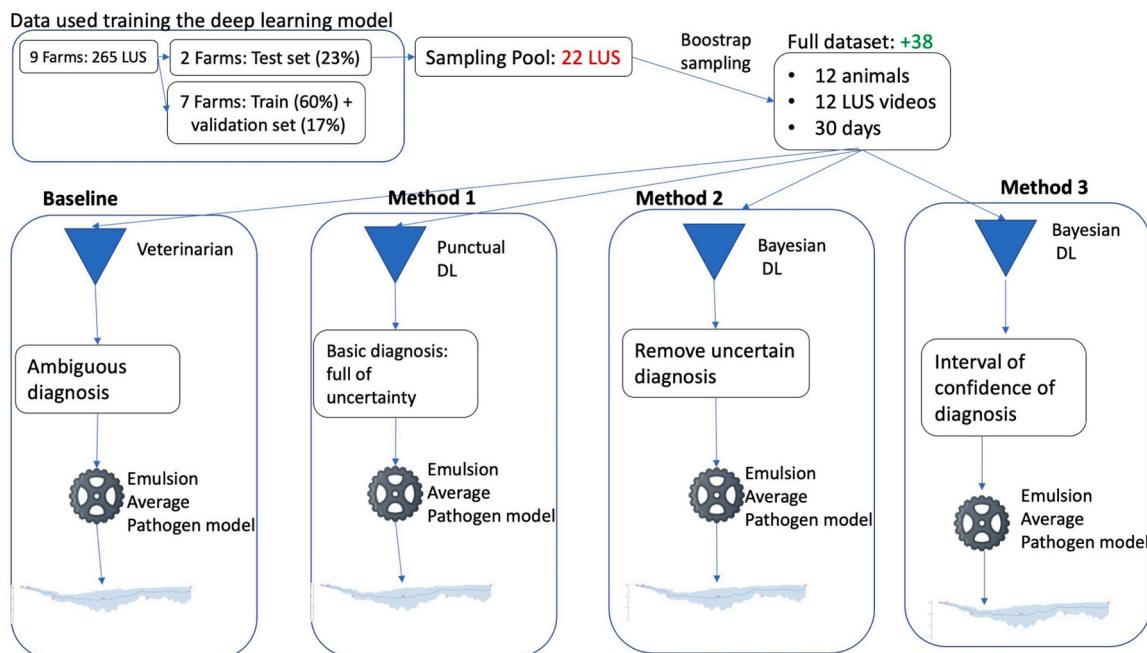


Fig. 5. Flow diagram depicting the data management process. One portion of the data was allocated for training and testing the deep learning model, while the remaining data was used to create a sampling pool. This pool was then utilized to generate a comprehensive dataset for evaluating the newly developed methods.

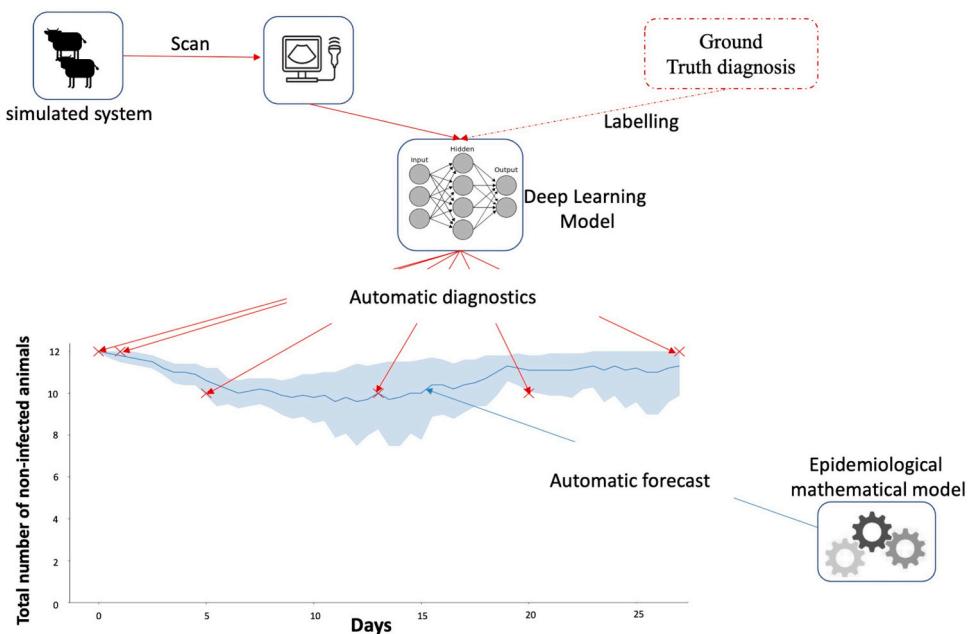


Fig. 6. Method 1 - Automating the traditional BRD study method. A deep learning model is trained on LUS videos and veterinarian examinations (utilized only during training) to provide punctual diagnoses of animals. These diagnoses are then used to parameterise three key epidemiological parameters of the average pathogen BRD mechanistic model using ABC inference. This approach enables automated diagnosis and forecast of the number of non-infected animal over a 30-day period.

2.4. Uncertainty-aware diagnostics

2.4.1. Uncertainty estimation

Method 1 integrates a data-driven model with a knowledge-driven model to automatically diagnose and forecast BRD. The output probabilities (softmax layer) from a deep learning model are often misinterpreted as indicative of model confidence, sometimes leading to

wrong predictions with high-confidence; A situation with potentially significant real-world consequences. What if we could enhance Method 1 to distinguish between risky and confident diagnostics, allowing experts to exploit the most informative predictions for crucial decisions-making, while applying supplementary examinations to challenging diagnostics? Model uncertainty refers to the inherent lack of confidence or certainty that a model may have in its predictions, acknowledging

that the model may not always be unequivocally certain about the correct answer. Various factors, such as limited data, data ambiguity, model complexity, and noisy data, can contribute to model uncertainty. A common strategy to quantify uncertainty in deep learning predictions is the use of Bayesian Deep Learning (BDL) models. Unlike traditional models, BDL treats model parameters as probability distributions rather than point estimates. This approach enables the model to offer not just predictions but also a posterior distribution representing the range of possible values. Incorporating this element of uncertainty provides a more nuanced understanding of the model's output. In BDL, the posterior distribution captures the model's updated beliefs about parameters after observing the training data, offering a valuable measure of confidence and variability in predictions.

In this study, we incorporated Monte Carlo Dropout (MCD), a previously established method to estimate deep learning model uncertainty (Gal and Ghahramani, 2016). MCD involves employing dropout during both training and testing phases in neural networks. During training, dropout randomly deactivates certain neurons, compelling the network to learn robust features and avoid over-fitting. During testing, the model is assessed multiple times with dropout enabled, leading to varying probabilities in the softmax layer based on the dropout rate (proportion of deactivated neurons). Instead of yielding a prediction with a fixed softmax probability, MCD produces a probability distribution for each class, with the predicted class being the one with the highest average probability (Bayesian model averaging). The uncertainty of the prediction is then quantified here by computing the Shannon entropy over the probability distribution of the classes. A higher entropy value signifies greater uncertainty, as the probability mass is spread across multiple classes. The Shannon entropy, introduced in deep Bayesian active learning, usually serves as an acquisition function, guiding the selection of training data with the highest uncertainty in hopes of enhancing model generalisation.

Following the implementation of a Bayesian approximation in our deep learning model, the final step is to determine the uncertainty threshold that optimally separates uncertain predictions from confident ones. This is achieved iteratively, evaluating the F1_score (harmonic mean of precision and recall) for each threshold value and identifying the value that maximises performance in the training set. The precision is also called the positive predictive value and the recall can be called the sensitivity.

2.4.2. Diagnostic filtering

Being able to obtain a prediction and its uncertainty level, we decided in this section to re-use the uncertainty to filter out noisy observations. [Algorithm 2](#) depict the given instructions to sample only noise-free observations. Understand here that by filtering out noisy observations, we are shrinking the original dataset. To simplify understanding, let's denote $I_t^{\text{filtered}} = \{N_1^{\text{filtered}, \text{infected}}, \dots, N_t^{\text{filtered}, \text{infected}}\}$ the space containing the count of infected animals in the filtered dataset per examination date t . C_t^{filtered} is the count of total animals (*infected + non-infected*) in the filtered dataset per examination date such that $N_t^{\text{filtered}, \text{infected}} \leq C_t^{\text{filtered}}$.

The code for the implementation is written in Python (Version 3.8), through the use of libraries of Tensorflow (version 2.15.0) and Keras (version 3.0.0) to build, train and evaluate the Bayesian deep learning architecture. Baal library (version 1.9.1) was used to implement filtering with the Entropy function. Optimization was also performed to find the best hyper-parameters using library KerasTuner (version 1.4.6).

2.4.3. Method 2

To conclude this section, we introduced a scenario ([Fig. 7](#)) where our Bayesian deep learning model performs batch diagnoses for all animals during each examination date. Following the batch diagnosis, we filtered out animals with excessively high uncertainty in the predictions.

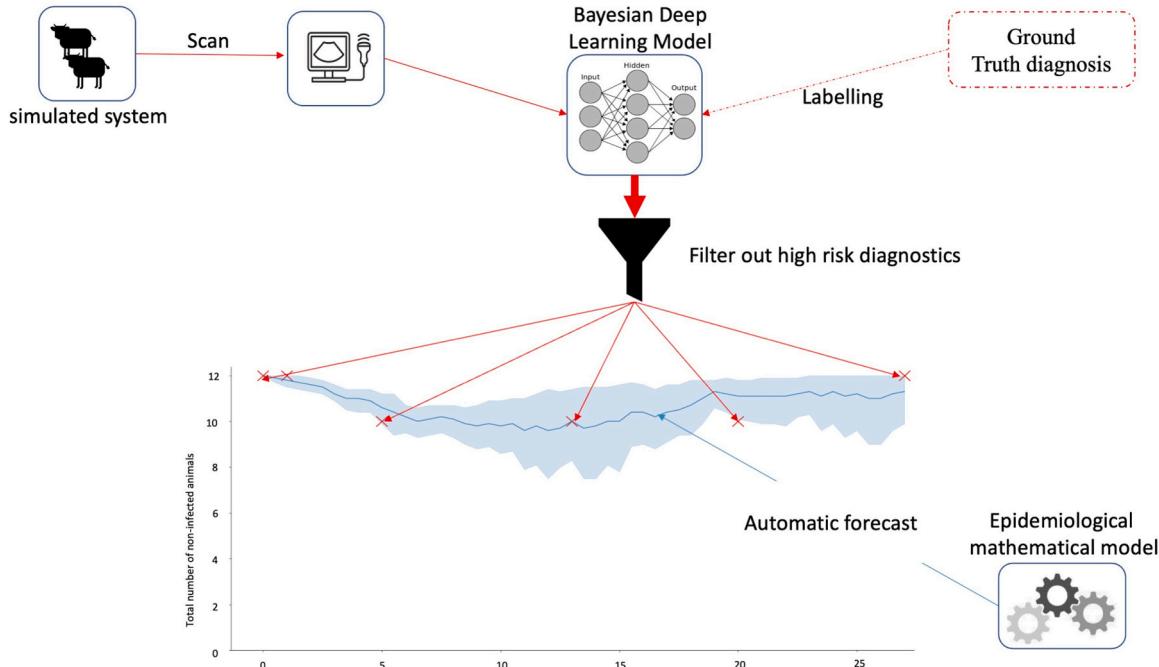


Fig. 7. Method 2 - Enhanced automated diagnostics through filtering. A Bayesian deep learning model is trained on LUS videos and veterinarian examinations (used only during training) to provide precise diagnoses with associated confidence levels. Low confidence diagnoses are flagged for further expert examination, while confident diagnoses are employed to parameterise the BRD mechanistic model. This approach ensures cautious diagnosis of the number of non-infected animal over a 30-day period.

Algorithm 2. Diagnostic adjustment through uncertainty-based filtering

number of infected animals around the predicted value. For simplicity, let's denote $G(\cdot)$ as the function that takes an LUS video input (x_t^{sim}) and predicts its infection state state ($y_t^{pred} \in \{\text{infected}, \text{non-infected}\}$) as a

Input : a scalar of the simulated LUS videos X_t^{sim} at each time step t

Output: a scalar of total approximated number of infected animals $I_t^{estimated, infected}$ at every step t

1 **Initialisation;**

2 **for** each time step t **do**

3 Get the total amount of initial animal $N_t^{observed, total}$;

4 Count of total prediction kept $C_{t-1}^{filtered} = 0$;

5 Count total infected animal filtered $N_t^{filtered, infected} = 0$;

6 **for** every x_t^{sim} in X_t^{sim} **do**

7 Diagnose using Bayesian deep learning $y_t^{predicted} =$

8 Get uncertainty of prediction $y_t^{predicted}$ s.t.
 $U(y_t^{predicted}) = \text{Shannon.} \text{Entropy}(y_t^{predicted})$;

9 **if** $U(y_t^{predicted}) \leq \epsilon$ **then**

10 Increment the total number of confident prediction, $C_t += 1$;

11 **if** $y_t^{predicted} == \text{infected}$ **then**

12 Increment number of infected prediction, $N_t^{filtered, infected} += 1$;

13 **end**

14 **end**

15 Get ratio of infected animals in filtered data, $R_t = \frac{N_t^{filtered, infected}}{C_t}$

16 Approximate the real number of infected animals,
 $I_t^{estimated, infected} \approx R_t \times N_t^{observed, total}$;

17 **end**

18 **end**

The ratio of infected animals in the filtered dataset was then used as an estimator for the true ratio of infected animals in the initial unfiltered dataset. This approach allowed us to obtain a revised diagnosis of the total number of infected animals per examination date. Similar to the scenarios outlined in the previous section, we used this new diagnostic to derive the epidemiological trajectory of the number of infected animals using the BRD mechanistic model. As in the previous section, we assessed the performance of this method (diagnosis, forecast, parameter inference) compared to the baseline, employing the same metrics as for method 1.

2.5. Uncertainty-aware deep mechanistic model

2.5.1. Ensemble estimator

Using a Bayesian deep learning model allows us to generate predictions along with associated uncertainties. In this section, these uncertainties were leveraged to establish a confidence interval for the

probability assigned to each class. Through the MCD technique, each execution of the Bayesian deep learning model on an input yields slightly different probabilities for each class. In the absence of noise in the input, the correct class will have the highest probability. However, with noisy inputs, the model may occasionally assign a higher probability to the wrong class.

In essence running a Bayesian deep learning model multiple times on a noisy input will, in most cases, predict the correct class, but occasionally, it may predict the wrong class. This implies that when $G(\cdot)$ is applied multiple times to all animals (x^{sim}) in a batch (X^{sim}), it does not consistently diagnose the same number of infected animals. Running $G(X^{sim})$ multiple times outputs a distribution of the number of infected animals $P(N_t^{infected})$ in the batch. From this posterior distribution, the confidence interval of the number of infected animals is derived, and the uncertainty of the diagnostics can be interpreted either as the variance of the distribution or its entropy.

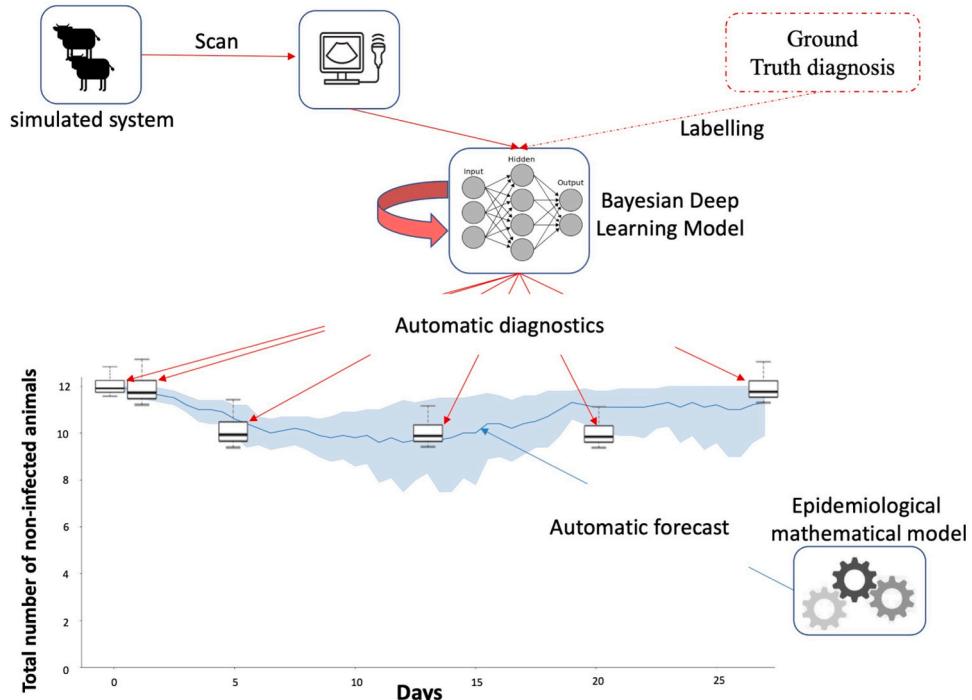


Fig. 8. Method 3 - Enhancing diagnosis and forecast through uncertainty propagation. A Bayesian deep learning model trained on LUS videos and veterinarian examinations (utilised only during training) provides an interval estimate of the total number of non-infected animals at different time steps. These diagnosis uncertainties are then propagated to the forecasting model (mathematical model), thereby enhancing its accuracy.

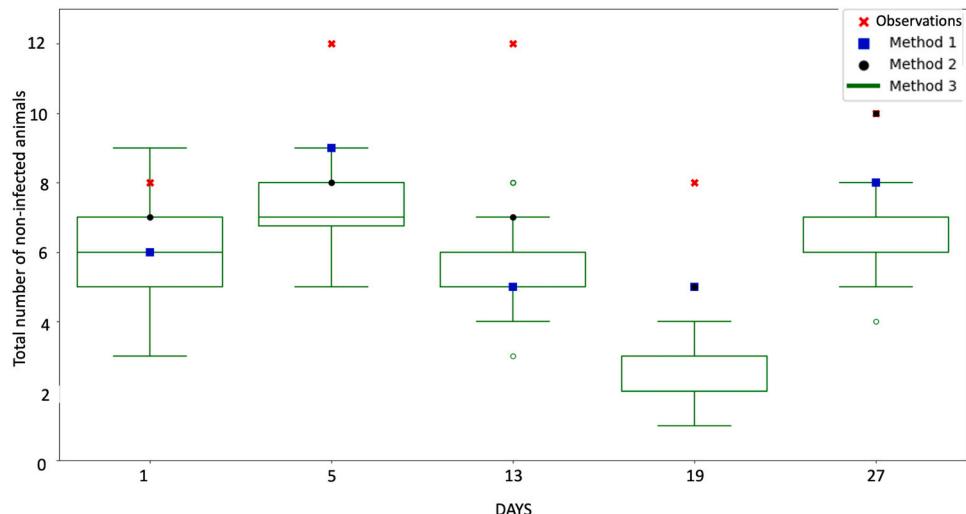


Fig. 9. Diagnostic performance comparison - Predicting the total number of non-infected animals in a farm batch at various observation dates. Methods 1, 2, and 3 employ Lung ultrasound videos as input, while baseline diagnoses are based on veterinarian observations, considered ground truth.

2.5.2. Method 3 - uncertainty propagation

In summary of this section, we formulated a scenario (Fig. 8) in which our Bayesian deep learning model forecasts a range of variation for the number of infected animals per examination date. The average prediction from the distribution of infected animals per examination date serves as the updated diagnostic. We compared this revised diagnostic with the baseline using the RRMSE. Furthermore, we introduced a step to incorporate the uncertainty from the revised diagnosis into the forecasting phase. During the parameter calibration of the mechanistic model, weights were assigned to each observation. The distance metric employed in the ABC-NN process is characterised by the weighted Euclidean distance, defined by the expression:

$$D_{\text{weighted}}(y^{\text{obs}}, y^{\text{sim}}) = \sqrt{\sum_{i=1}^n w_i (y_i^{\text{sim}} - y_i^{\text{obs}})^2}$$
 Where, y^{obs} is the revised diagnostics, y^{sim} is the simulated diagnostics (by the mechanistic model) and w_i is the weight of the revised diagnostics expressed as the variance of distribution of repeated batch diagnostics. The forecast performance of the mechanistic model fitted with in this scenario was compared to that of the baseline using the RRMSE metric. Similarly, the estimated parameters were also compared with those of the baseline.

3. Results

Results are organised as follows: first, we compared the diagnostics performance of each method (1, 2, 3) to that of the baseline method.

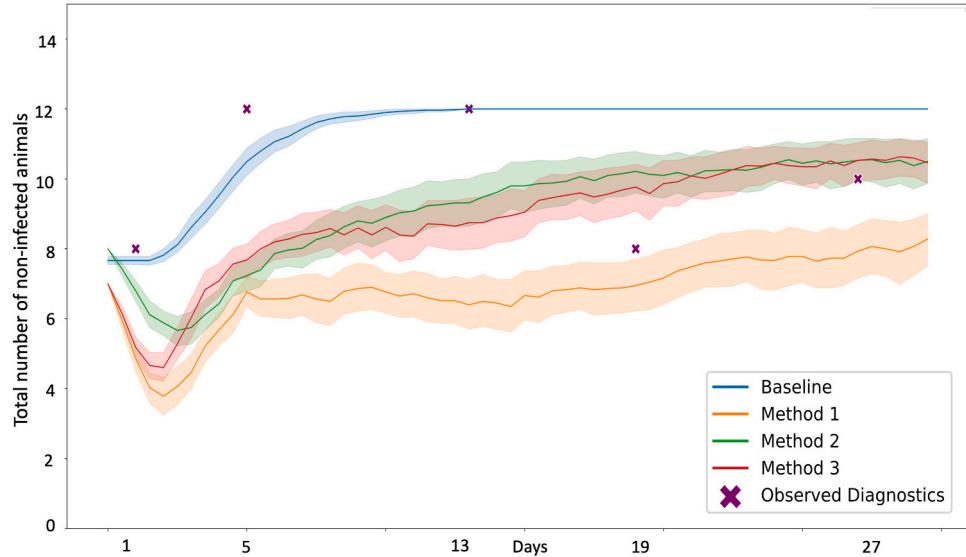


Fig. 10. Forecast Performance Comparison: predicting the progression of non-infected animals in a batch over 30 days. Ground truth diagnostics (cross) are based on veterinarian examination. Baseline forecast is fitted to ground diagnostics, while methods 1, 2, and 3 are fitted to their respective diagnoses (paragraph 3.1).

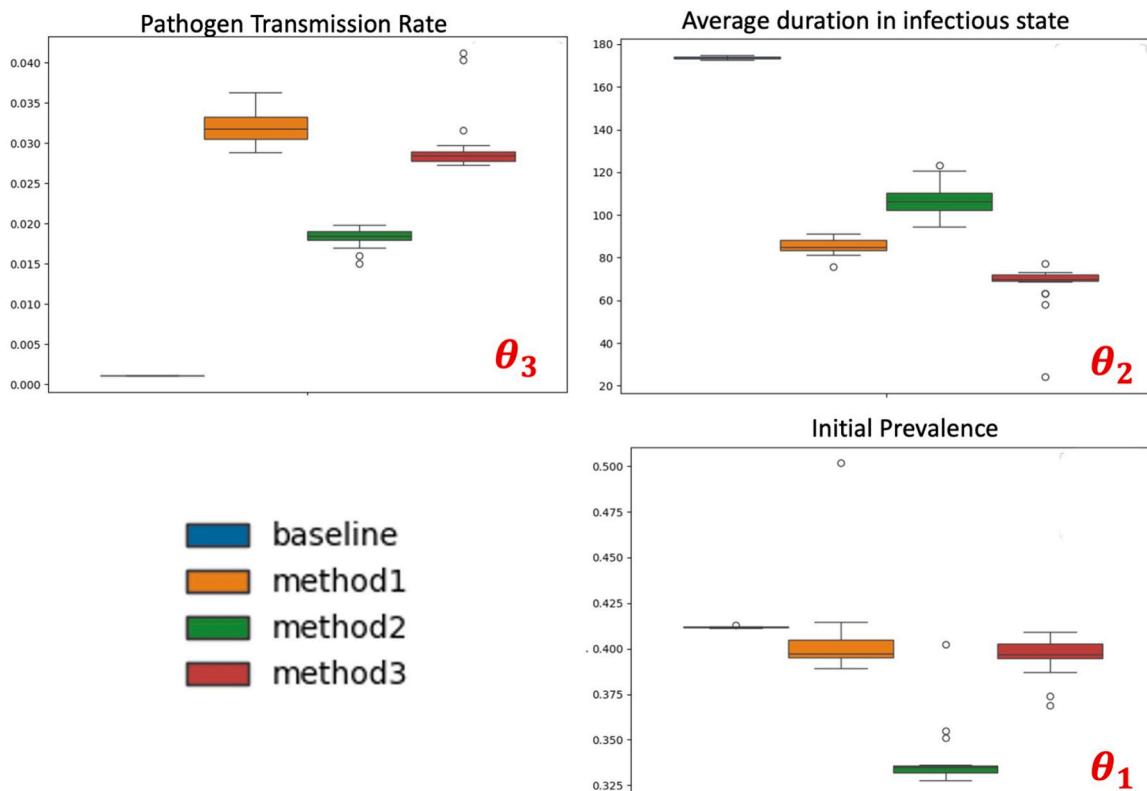


Fig. 11. Parameter inference performance comparison - Estimated distribution of pathogen transmission rate θ_3 , average duration in infectious state θ_2 , and initial prevalence θ_1 across methods. The goal is to be as close as possible to this baseline.

Secondly, we compared the forecast of each method to that of baseline. Third we compared the value of the epidemiological parameters of each method to that of the baseline.

3.1. Diagnostics

Applying each method presented in Section 3, 4, 5 to diagnose the total number of infected animals in a batch at different time step yield different results. Fig. 9 illustrates the diagnostic performance for each

method compared to the baseline: baseline diagnostics (represented by crosses) are supposedly the most confident diagnostic that can be obtained, they were established based on veterinarians' examinations (clinical and biological). Method 1 (represented by squares), where a deep learning model is used as a punctual estimator, yields the highest errors compared to the baseline diagnostics with a RRMSE of 39 %. Note here that the deep learning model in itself after optimisation obtained a F1_score of 72 %. Method 2 (black dots), where the uncertainty of a Bayesian deep learning model is used to improve its predictive

performance, yields the lowest diagnostic errors compared to the baseline with a RRMSE of 32 %. In, method 3 (box-plots), where a bayesian deep learning model is used to diagnose in the form of an interval of variation, it is the mean of the interval that is used final value and which is compared to the baseline diagnostics. Method 3's performance is equivalent to that of method 2.

3.2. Forecasting

Applying method 1, 2, 3 to forecast using their previous diagnostics yield different results.

Fig. 10 illustrate the performance obtained for each method tested. The forecast of each method was fitted to their respective diagnostics (**Fig. 9**), note that for method 3, its forecast was adjusted to the mean diagnostic (from the box-plot). The ultimate goal here is to obtain forecasts that are the closest to the baseline. Method 1, where diagnostics are estimated using a deterministic predictor yields the worst results with an RRMSE of 38.4 %. method 2 and 3, where the uncertainty (or confidence) of each diagnostic is evaluated and re-used, yields the best results with an RRMSE of 27.2 %. The performance of method 2 and 3 is close to the baseline forecast (which was fitted on veterinarian diagnostics) the RRMSE is 23 %.

3.3. Parameter inference

The infectious dynamic (forecast) obtained for each method is characterised by different parameter values. These parameters represent epidemiological phenomenon's.

Fig. 11 illustrates the estimated parameter values for each method. The pathogen transmission rate, an epidemiological parameter indicating how rapidly a disease spreads among animals, is closest to our reference values (baseline) when using method 2. Similarly, the average duration in the infectious state, describing the period during which an infected animal can transmit the disease, aligns closer with our baseline when estimated using method 2. Initial prevalence refers to the proportion of infectious animals at the outbreak's onset. Interestingly, methods 1 and 3 demonstrate better estimation accuracy than method 2 in this regard. Despite similar forecast performances between methods 2 and 3, their estimated parameters differ significantly. BRD was an example of application of our methodology.

4. Discussion

4.1. Data acquisition process

In our experimental protocol, we structured our sampling periods ($t \in 1, 5, 14, 21, 28$) and selected animals for examination based on constraints posed by the availability of farmers and veterinarians. Due to these limitations, we were unable to collect data from every animal, leading us to employ bootstrap sampling to generate a comprehensive dataset. Despite this challenge, bootstrap sampling provided us with the most objective approach to ensure dataset completeness, given the circumstances. The encouraging results obtained might incite end-users to modify the experimental sampling protocol accordingly. Deep learning performances are proportional to the size of the training set. Hence scaled up to commercial herds, if including a new training phase, should in theory lead to better performances. But if complete herds were not going to be scanned, how animals might be prioritised amongst the herd is a trickier question. By analogy with standard active learning techniques (Settles, 2009) like query-by-committee, one could rely on inter raters' disagreement on clinical signs for such animal selection. The idea for such selection is that the less the raters agree on the status of a certain individual, the more information this individual will give about the frontier between (health) states. Hence, animals could be chosen for biological and scan exams according to maximum inter raters' certainty (healthy or not) and uncertainty (to try to find the best discrimination

between states).

Regarding the sensors used, we relied on lung ultrasound videos, a tool highlighted in the literature (Ollivett and Buczinski, 2016; Timsit et al., 2019) for its efficacy in quickly identifying caudal lung lobe consolidation, lung necrosis, and lung abscessation. However, certain limitations should be acknowledged. Only lesions adjacent to the pleura lines were visible, thereby restricting visibility of deeper lesions. Animals underwent TUS on both sides of the thorax in 6 out of 9 farms. However, in the remaining 3 farms, this was not feasible due to the type of restraint used. Within the local farming system, it was challenging to establish a recruitment criterion that mandated access to both sides of the thorax, alongside other criteria such as internet access and a sufficient number of animals purchased annually. We acknowledge this as a limitation, as previous studies in calves have demonstrated relatively low agreement between consolidations observed on one side of the thorax versus the other (kappa value = 0.33) (Buczinski et al., 2014). Similarly, in our study, when evaluating TUS results from the first day consolidations were detected in an animal, the agreement between the two sides of the thorax was low (kappa value = 0.30). Additionally, discerning whether observed consolidations are active or old (scarred) tissues (Masset et al., 2022) remains challenging. Furthermore, our access was restricted to a fairly caudal part of the lung (from the 4th intercostal space), but we know that lesions typically originate in the cranial part (Masset et al., 2022), potentially leading to delayed diagnosis. We hypothesised that an infected animal could have at least one pathogen detected in the cranial part, but depending on the pathogen, lung damage might not always be visible (as the pathogen may remain only in the upper respiratory tract) or could be delayed, potentially resulting in false negatives. To address these limitations, future research could explore integrating various sensor data types, such as video surveillance for behavioural observation, audio recordings for detecting acoustic events (e.g., coughing, sneezing), and environmental parameters like CO₂, NH₃, and temperature. By incorporating multi-modal data simultaneously, akin to a veterinarian's holistic evaluation (visual, auditory, environmental), we could provide a more comprehensive assessment of an animal's health. Video surveillance coupled with audio surveillance seems particularly promising due to their synchronised nature and ability to capture the entire batch of animals more frequently than lung ultrasound examinations. This would enable synergy between complementary sampling methods, relatively a specific but continuous (surveillance) and specific but only punctual (ultrasound).

In any case, whatever the sensor or sampling method, establishing a consensus on ground truth data remains challenging due to the absence of a clear gold standard (Timsit et al., 2016). In this study, we defined rules for diagnosing the infectious state of animals, considering an animal infectious if it harboured at least one pathogen during PCR examination. However, this approach carries inherent risks, as not all pathogens play equal roles (Gershwin et al., 2015), potentially leading to an elevated rate of false positives. Addressing this ambiguity in ground truth labelling, recent work has introduced conformal prediction under ambiguous ground truth (Stutz et al., 2023), leveraging multiple expert opinions for uncertainty quantification. Employing such methods with clinical and biological outcomes, even when they disagree, holds promise for enhancing diagnosis accuracy.

4.2. Automatic diagnostics

Pre-processing data for deep learning models poses inherent challenges, and in our study, we addressed this by adopting a downsampling strategy, randomly removing labels to achieve a balanced dataset. However, we recognise that this approach is sub-optimal as it may result in the loss of information. To overcome this limitation, we propose the application of active learning (Gal and Ghahramani, 2016), a technique where algorithms actively select the most informative inputs from a large pool of unlabelled data for annotation by a human annotator. This method has demonstrated effectiveness in enhancing the performance of

deep learning models, particularly when dealing with highly imbalanced datasets (Lee and Seo, 2022).

Our work proves the importance of evaluating the confidence level of predictions for diagnosis and forecast. As future research could integrate multiple types of sensor data, automatic diagnostic models must adapt to accommodate multi-modal approaches. To our opinion, the most promising way forward is to employ deep audio-visual learning model (Zhu et al., 2020). It could be a promising avenue for enhancing diagnosis accuracy and forecast capabilities in such multi-sensor environments as it treats audio-visual problems as a whole not as separate parts, audio and visual.

4.3. Forecasting

In our current understanding, only two epidemiological mathematical models have been published in the literature. The first model was introduced in 2019 (Picault et al., 2019a), followed by the second model in 2023 (Sorin-Dupont et al., 2023). In this study, we employed the first model, which was calibrated under the assumption of an "average pathogen" infection to maintain simplicity. Despite parameterising this model using veterinarian diagnoses (considered the most confident values), we observed a relative average forecast error of 23 %. This discrepancy may be attributed to the multi-pathogen nature of BRD, where the prevalence of each pathogen and their interactions can significantly influence infection dynamics. To address this complexity, future research could explore the adoption of a pathogen-specific model (Sorin-Dupont et al., 2023), offering a more nuanced understanding of BRD dynamics. In our study, the epidemiological mathematical model was parameterised through an inference process using Approximate Bayesian Computation algorithms. We incorporated uncertainties of observational points (diagnoses) into the process, enhancing forecasts by weighting each diagnosis according to its confidence level, expressed as variance. While the inclusion of rules within the mathematical model has contributed to error reduction, there remains a need to enhance the integration between observational data, their confidence levels, and the mathematical model. For instance, ABC is only one of many likelihood-free methods (Drovandi and Frazier, 2022) that we could adapt to take advantage of uncertainty-awareness in the deep learning predictions, hopefully leading to even more accurate and reliable forecast.

5. Conclusion

This study represents a pioneering effort in leveraging sensor data, particularly lung ultrasound videos, to cautiously diagnose and forecast the progression of BRD in a batch. Our method is versatile as it does not rely on specific sensor types or disease characteristics, making it applicable across various contexts where early detection is challenging. While acknowledging the imperfections in our data acquisition protocol, the findings of this study highlight a functional coupling method. To render it operational for the study of Bovine respiratory Disease, it is imperative to improve the data acquisition protocol.

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Declaration of Competing Interest

The authors declare no conflicts of interest.

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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).

Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.prevetmed.2024.106354.

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Chapter 5

General discussion

5.1 Main contributions

Integration of sensor-based and mechanistic models Central methodological contribution of this thesis is the integration of deep learning diagnostic tools with mechanistic epidemiological models to improve disease management, specifically for bovine respiratory disease (BRD). This hybrid AI-epidemiological approach explicitly tackles the challenge of reconciling short-term, sensor-driven diagnostic accuracy with long-term, model-based epidemiological forecasting. We drew inspiration from the Mixture of Experts paradigm by loosely coupling two specialized components – one for diagnosis and one for prognosis – and assigning each to its domain of expertise. This design allowed deep learning to focus on immediate, data-driven classification of disease status, while the mechanistic model provided reliable long-term projections based on epidemiological principles. The approach demonstrated two key strengths. First, the deep learning module excelled at rapid, accurate diagnosis from noisy sensor data (lung ultrasound imagery), even with limited training examples. For instance, the model achieved about 72% classification accuracy using fewer than 30 training ultrasound video samples, highlighting its practicality in data-scarce veterinary settings. Notably, when we enhanced this diagnostic model with a Bayesian architecture to quantify prediction confidence, the effective accuracy rose to roughly 88% by filtering out highly uncertain cases – an improvement that underscores the value of uncertainty-aware AI in automating complex clinical assessments [201]. Second, the mechanistic epidemiological module excelled at prognosis: it extended the short-term diagnostic insights into accurate long-term forecasts of disease dynamics. After parametrising the model with empirical BRD outbreak observations, it produced robust epidemic trajectory predictions with a forecast error (RMSE) below 10%. This level of accuracy demonstrates the mechanistic model’s value for strategic decision-making over longer time horizons, complementing the immediacy of the deep learning diagnoses. By systematically separating diagnostic and prognostic tasks, our hybrid framework capitalizes on the respective strengths of data-driven AI and mechanistic modelling, an approach aligned with recent calls to combine these paradigms for epidemic prediction. Overall, this integration of sensor-based AI and mechanistic modelling is an innovative step toward decision-support tools that operate across temporal scales of disease management [202].

Explicit handling of uncertainty A second major contribution of this work is the explicit quantification and propagation of uncertainty within the hybrid diagnostic-prognostic pipeline. We addressed the question of how to manage the significant uncertainty inherent in BRD sensor data

(noisy ultrasound observations of pathological lung changes) through a Bayesian Deep Mechanistic approach. By employing Monte Carlo Dropout for variational inference, the deep learning model generated probabilistic predictions along with measures of confidence [57]. We then filtered out the most uncertain diagnoses – essentially having the system “know what it doesn’t know” – which yielded a notable reduction in diagnostic error rates (from an initial relative RMSE of 39% down to 32%). These uncertainty-filtered predictions were subsequently used in the mechanistic model’s calibration via a weighted approximate Bayesian computation scheme, so that less certain inputs were given diminished influence. Propagating the diagnostic uncertainty in this manner improved the reliability of long-term forecasts: the hybrid model’s projection error dropped to a relative RMSE of 27.2%, approaching the 23% error of a baseline model informed by expert veterinary diagnoses. In other words, our framework better matched expert-driven forecasts by embracing uncertainty rather than ignoring it. This result is significant because it shows that a principled treatment of uncertainty can enhance both immediate and future predictions in disease monitoring systems. The outcome supports recent observations that accounting for prediction confidence improves epidemiological forecasts. Importantly, this contribution tackles real-world complexity: livestock health data are often limited or imperfect, and by embedding uncertainty into the decision pipeline, our approach maintained robust performance even when data quality was compromised. This methodological advance – integrating Bayesian deep learning with epidemiological simulation – directly confronts the need for reliability in AI-driven agriculture, ensuring the system remains cautious and reliable under data ambiguity.

Pathogen identification via model-based distinguishability Another key innovation of this thesis is a method to identify the likely causative pathogen of BRD from clinical observations, using mechanistic models and simulation-based inference. We introduced a pathogen-specific modeling framework in which distinct mechanistic epidemic models were formulated for different BRD etiological agents – specifically, Orthopneumovirus (BRSV), Mannheimia haemolytica, and Mycoplasma bovis. Using approximate Bayesian computation combined with multinomial logistic regression as a model selection tool, we were able to discriminate among these candidate pathogen models based solely on early symptomatic trajectories. This approach achieved high identification accuracy (93% on average, with individual pathogen identification rates of about 87–96%). Such performance demonstrates that even when different pathogens cause clinically overlapping respiratory syndromes, their dynamical “fingerprints” in outbreak data can be teased apart with the right analytical approach. This contribution is particularly noteworthy because coinfections and similar clinical presentations are common in BRD [203], making targeted interventions difficult in practice. By focusing on model distinguishability – ensuring each pathogen’s model produces sufficiently unique patterns – our method provides a data-driven way to infer the likely infection cause. This is an important step toward pathogen-specific decision support. Unlike traditional diagnostic tests which might require lab work or specific assays for each pathogen, our approach uses routine observational data (e.g. clinical scores over time) to probabilistically identify the pathogen. This opens the door for earlier and more tailored treatments. In summary, we demonstrated a novel use of simulation-based inference for epidemiological model selection in an animal health context, aligning with emerging applications of ABC in infectious disease modelling [204].

Coupling with bio-economic modelling and decision support We extended our framework beyond biological predictions by integrating economic analysis, thereby linking epidemiological outcomes to tangible farm management metrics. Specifically, we coupled the outputs of our mechanistic BRD models (such as predicted number of cases under different interventions) with a farm profitability model that accounts for treatment costs, animal performance, and other economic factors. Through this integration, we evaluated the real-world impact of using pathogen-informed

strategies versus conventional blanket treatments. The results indicated that tailoring interventions to the identified pathogen could substantially reduce antimicrobial usage – by approximately 44% in our simulations – without sacrificing economic performance. In fact, the optimized, information-driven strategy slightly increased net profit (1% higher) compared to traditional empirical treatment regimens. These findings carry practical significance. They suggest that better diagnostic-prognostic information can enable win-win scenarios in livestock health: improving animal welfare and public health (through judicious antibiotic use) while maintaining or even enhancing farm profitability. This bio-economic coupling illustrates the concrete benefits of our hybrid methodology. It moves the contribution from a purely methodological realm into one that resonates with industry and societal goals, like combating antimicrobial resistance (AMR) in agriculture [205]. By quantitatively showing that informed decisions can reduce antibiotic use with minimal economic penalty, our work provides evidence in favour of precision medicine approaches in veterinary practice. Moreover, incorporating economic considerations forces the model to focus on outcomes that matter to farmers and stakeholders, enhancing the relevance of our research for real-world adoption. This interdisciplinary integration of epidemiology and economics is still uncommon; thus, our thesis contributes a template for how to merge disease modelling with cost-benefit analysis to guide actionable recommendations.

Structured modularity and methodological scalability Finally, an essential contribution of this thesis is the modular design of the hybrid modelling framework, which emphasizes clear separation between components and hence greater interpretability and flexibility. We deliberately maintained independent modules for (i) sensor-based diagnosis via deep learning, (ii) disease progression and prognosis via mechanistic models, and (iii) outcome evaluation via economic modelling. This weak modularity (weakly coupled) means that each module can be developed, fine-tuned, and validated by domain experts relatively independently – for example, veterinarians and epidemiologists can focus on improving the mechanistic model or its parameters, while computer scientists can refine the deep learning model, without constantly retraining a monolithic system. This is in contrast to end-to-end integrated approaches like EAAMs, which entangle data-driven and mechanistic components into a single architecture. The modular design also eases adaptation to new contexts or updates. For instance, if a new diagnostic sensor becomes available or a new pathogen emerges, one can update or swap out the relevant module (diagnostic or mechanistic) without overhauling the entire system. This feature is especially attractive in agriculture settings where conditions vary widely: the framework could be reconfigured for a different species or management system by exchanging modules while preserving the overall architecture. This emphasis on modular, plug-and-play components aligns with software engineering best practices and is conducive to multi-disciplinary collaboration. Different teams (data scientists, veterinarians, economists) can work in parallel on their piece of the puzzle, which is crucial in an interdisciplinary project. In summary, the thesis not only delivered specific models and results, but also a methodological template for hybrid modelling that is interpretable, extensible, and generalizable. This approach could help bridge the gap between experimental AI models and practical decision-support tools in agriculture, where stakeholder trust and adaptability are paramount [206].

5.2 Limitations

Despite the above contributions, several limitations of our current work must be acknowledged. These limitations point to areas where further research and development are needed, and they temper the interpretation of our results. We discuss the main bottlenecks in turn, focusing on data inputs, model coupling, validation, and practical deployment challenges. It should also be noted

that some of these limitations arise inherently from the interdisciplinary nature of the project – spanning animal health, machine learning, and farm management – which requires balancing competing considerations.

Data input limitations (sensor and observations) A fundamental limitation lies in the reliance on thoracic ultrasound (TUS) as the primary sensor input for the diagnostic module. While lung ultrasound imaging was chosen for its practical relevance (it provides a direct non-invasive view of lung lesions and consolidation in BRD cases), it only captures one aspect of the animal’s health state. Pulmonary ultrasound, as valuable as it is, offers an incomplete picture of respiratory disease. For example, severe lung lesions can sometimes be missed if they do not contact the pleura or if they occur in lung regions not accessible to ultrasound scanning. Studies have shown that traditional clinical examinations like auscultation often fail to detect such lesions altogether, and TUS is much more sensitive in that regard [207]. In feedlot cattle, Timsit [195] demonstrated that the maximal depth and area of lung consolidation visible on ultrasound at the time of diagnosis are significantly associated with increased risk of BRD relapse and with reduced weight gain. This evidence underpins our use of ultrasound as a prognostic indicator. Likewise, on-farm studies [194] have advocated TUS as a useful tool to identify poor prognostic signs such as extensive lung lobe consolidation or abscessation in calves, which can guide culling or intensified treatment decisions. However, focusing on ultrasound alone means our diagnostic system could overlook clinical signals of BRD that manifest in other modalities (e.g. fever, coughing, nasal discharge, or behavioral changes). For instance, a Scottish study in sheep found that relying on auscultation alone missed many cases of pneumonia that ultrasound or necropsy would catch, indicating that each modality has blind spots. In our case, the limitation is that using only ultrasound-based features might lead to false negatives (disease not detected if lesions are not visible on the pleural surface) or false positives (lesions due to past infection or other causes). This in turn would affect the accuracy of both the diagnosis and the downstream prognostic recommendations. In a real veterinary setting, a clinician examines the animal holistically – looking at physical demeanour, nasal/ocular secretions, listening for coughs or abnormal lung sounds, measuring temperature, etc. Our current approach does not yet incorporate these additional data streams. Therefore, a more multimodal sensing strategy is warranted. Combining multiple sensors (visual, acoustic, thermal, etc.) could give a more complete view of the disease state and mitigate the reliance on any single observation type. The need for multimodal data integration is underscored by evidence that certain BRD cases present predominantly with behavioural changes (e.g. feed intake reduction) or audible symptoms (frequent coughing) that might precede ultrasound-detectable lesions [208]. In summary, the limitation is not the ultrasound modality per se – which is in fact quite informative – but the exclusivity of its use. Expanding the observational input to include, for example, automatic cough monitors, could improve detection sensitivity and specificity. Our current dataset was also relatively limited in size and scope (few farms and conditions), which might limit the generalizability of the trained diagnostic model; larger and more diverse datasets are needed to ensure the model’s robustness across different herd management conditions.

Proxy-based coupling and uncertainty modelling Another methodological limitation concerns how the deep learning outputs are integrated into the mechanistic model – what we termed a proxy-based hybrid approach. We used the deep learning model to generate a proxy indicator (the probability of infection in the group) which then feeds into the mechanistic simulation. While intuitive, this coupling can be fragile. It assumes that the learned proxy is a reliable summary of the complex infection state, and any error or bias in the proxy will propagate to the prognosis. We partially addressed this by incorporating the model’s uncertainty (via variational Bayesian methods) into the coupling: uncertain predictions were down-weighted during mechanistic calibration. How-

ever, the uncertainty quantification method itself has limitations. We relied on Monte Carlo dropout to approximate Bayesian uncertainty in the deep network [57]. This method provides an estimate of model uncertainty and has the advantage of easy implementation, but it optimizes for average-case performance and does not guarantee calibrated uncertainty intervals [209]. In practice, we observed that our Bayesian neural network sometimes remained over-confident or under-confident in certain scenarios. For example, some lung ultrasound videos classified as positive (diseased) with high confidence turned out to be false alarms, partly because the ground-truth labeling by veterinarians is subjective and can be ambiguous (there is no perfect gold standard test for subclinical BRD). The Bayesian neural network’s predictive intervals did not always capture these ambiguities – a limitation because it means that simply having a high model confidence isn’t a foolproof indicator of correctness [210]. Moreover, the Monte Carlo dropout approach can become computationally expensive and may not scale well to more complex deep learning architectures. Recent advances like Transformers [50] have shown superior performance in many pattern recognition tasks, including medical imaging, but applying Monte Carlo sampling to such large models would be costly and may still yield poorly calibrated uncertainties. In summary, while our incorporation of uncertainty is a strength of the thesis, it is not the final word on the matter. The limitation is that our current uncertainty modelling may not fully guarantee that the “right” decisions (e.g., whether to trust a particular model prediction) are always made. In future iterations, alternative uncertainty quantification techniques (such as conformal prediction to generate guaranteed coverage prediction sets, or Bayesian neural networks with better priors) should be explored to overcome this limitation. Additionally, our hybrid model currently treats the deep learning output as a static proxy; a tighter integration (for instance, a joint inference over parameters of both models) could potentially improve coherence between diagnosis and prognosis, though this comes at the cost of a much more complex inference procedure.

Validation using simulated vs real field data Some of our findings, particularly those related to optimal control strategies and pathogen-specific interventions, were derived from simulated outbreak scenarios rather than extensive field trials. This reliance on simulation is a practical necessity – it would be infeasible to experimentally trial different pathogen-specific interventions on real farms within the PhD timeline – but it constitutes a limitation in terms of validation. We showed theoretically (in Chapter 3) that the mechanistic model, when given early infection data, can differentiate between pathogens and inform decisions like whether to use a virus-specific treatment or a bacterium-specific antibiotic. These simulations included realistic stochastic variability and indicated significant potential benefits (less antibiotic use, maintained performance). However, real-world BRD outbreaks can be more complex. Multiple pathogens often circulate simultaneously or sequentially in the same group of animals [203], and subclinical infections can go undetected. The interactions between co-infecting agents (viral and bacterial) may alter disease dynamics in ways not fully captured by our set of discrete pathogen-specific models. For instance, concurrent infections could lead to atypical progression or different treatment responses that the model, which assumes a single dominant pathogen at a time, might not predict. Furthermore, farmer interventions (such as metaphylactic antibiotic treatment or vaccination) in real settings are not as controlled as in our simulations, potentially introducing deviations from model assumptions. In short, there is a gap between simulated performance and field performance of the system. This thesis did not include a longitudinal field trial to empirically confirm that using our hybrid diagnosis-prognosis system leads to better outcomes than status quo decisions. The lack of field validation means that conclusions about management benefits should be interpreted cautiously. For example, the predicted 44% reduction in antibiotic use assumes perfect adherence to model recommendations and accurate pathogen identification by the model. In practice, there may be cases where the model’s recommendation is not followed or is misinformed by unusual data, which could reduce the realized benefit. This lim-

itation points to the need for future empirical studies: deploying the system on farms to measure its impact on decision-making, disease outcomes, and economic returns. Until such validation is done, our results remain promising indicators rather than proven outcomes. We have taken steps to ensure realism in simulations (e.g., including variability and noise), but empirical calibration against real outbreak data is needed to fine-tune model parameters and to build confidence in the system's recommendations under practical conditions.

Interdisciplinary and deployment challenges A further set of limitations arises from the interdisciplinary scope of the project, which brings together expertise from veterinary science, computer science, and agricultural engineering. One issue was the definition of ground truth for training and evaluation. In the absence of a single definitive diagnostic test for BRD, we relied on veterinary clinical assessments (symptom scoring, etc.) as proxies for ground truth labels (infected vs. healthy). However, even experienced veterinarians can disagree on borderline cases, and as noted, BRD is a syndrome with no unique biomarker. This label noise likely impacted the training of our diagnostic model – a limitation common in medical AI applications where labels are imperfect [211]. Disagreements over what constitutes “disease presence” introduced uncertainty not only in the model but also among the team members interpreting results. Better approaches to handle ambiguous labels (such as probabilistic labels or consensus labelling) were not fully implemented in this thesis. Another challenge was meeting the diverse expectations of stakeholders. Farmers ideally want a tool that is easy to use, provides clear recommendations, and improves their bottom line. Veterinarians want the tool to be trustworthy, aligning with their clinical intuition and not missing critical cases. Industry partners (e.g., ag-tech companies) are concerned with feasibility: is the system fast and reliable enough, cost-effective, and integrable into farm workflows? Our prototype system, while scientifically promising, is still a proof-of-concept. Usability and integration limitations include the need for continuous data connectivity (ultrasound data had to be uploaded to a server for analysis), the time taken to run analyses (which currently may not be real-time in field conditions), and the requirement for relatively sophisticated hardware (ultrasound machines, GPU servers for the AI model, etc.). In a practical deployment, decisions such as on-device (edge) vs. cloud computing must be addressed to ensure timely feedback to the farmer. We partially addressed this by setting up a basic communication pipeline: for example, audio recordings were transmitted from on-farm sensors to a central server for processing. However, this is only an initial step. We did not fully optimize the system for latency or energy consumption – important factors if devices are battery-powered or connectivity is intermittent. Additionally, the current system would require a technician or vet to perform ultrasounds on calves, which is an extra labour step. Automating or simplifying data collection (perhaps using fixed sensors or self-service kiosks for animals) is another practical hurdle. In summary, the limitation here is that significant work remains to turn the research prototype into a deployable product. This includes improving the user interface, ensuring the analysis can run with minimal user intervention, establishing reliability and fail-safes (what if a sensor fails or gives implausible data?), and conducting training for end-users. The interdisciplinary nature of the project, while a strength, also meant we had to navigate different terminologies and priorities, which occasionally slowed progress or led to compromises in design. These challenges emphasize that technical innovation alone is not sufficient – understanding the context of use is crucial. The thesis lays the groundwork, but a concerted effort with input from farmers, veterinarians, and engineers will be needed to refine the system. Only by doing so can we overcome the last-mile limitations and ensure the tool is accepted and effective in real decision-making scenarios.

5.3 Perspectives

Building on the contributions and acknowledging the limitations discussed, several avenues for future work emerge. These perspectives encompass methodological enhancements and broader explorations to increase the impact and applicability of our hybrid AI-epidemiological framework. We outline key future directions in terms of model improvements, uncertainty handling, inference techniques, decision-making integration, comprehensive validation, and domain transfer. Each of these is aimed at addressing current limitations and pushing the boundary of what such hybrid systems can achieve in animal health management.

Integration of multimodal deep Bayesian mechanistic models A natural extension of this work is to incorporate multiple sensor modalities (e.g. visual and auditory data) into a unified diagnostic-prognostic framework. In current practice, veterinarians assess BRD using a combination of visual cues (signs of fatigue, nasal discharge, posture) and auditory cues (frequency and nature of coughing, lung sounds) alongside ultrasound findings. Our system could be expanded to emulate this holistic assessment by fusing data from cameras and microphones in addition to ultrasound. Recent developments in deep learning provide methods for audio-visual learning that could be leveraged to this end [212]. For example, an audio analysis model could continuously monitor cough sounds in the barn, which are a strong indicator of respiratory distress [213]. By aligning cough event data with visual health indicators and ultrasound results, we might improve early detection sensitivity – catching cases that ultrasound-alone diagnostics could miss. However, integrating heterogeneous data streams poses significant challenges: synchronization of signals (timing coughs to specific animal observations), dealing with noise (barn acoustics can be poor, and visuals can be affected by lighting or occlusion), and learning an effective joint representation. Advanced techniques like audio-visual attention mechanisms or representation learning could be applied so that the model learns cross-modal features (e.g., linking an increase in cough frequency with subtle changes in animal posture or ultrasound anomalies). Audio-visual separation methods might help isolate meaningful sounds (coughs vs. background noise) in realistic farm environments [208]. Future research may implement a multimodal Bayesian mechanistic model, wherein each modality contributes to an overall belief about the herd’s health state, and uncertainties from each sensor are combined. Importantly, incorporating new modalities will require new data – potentially a large labeled dataset of concurrent audio, video, and ultrasound recordings of calves. Obtaining such data is non-trivial, and data annotation becomes a bottleneck. Here, techniques like weakly-supervised learning and active learning could prove invaluable. Rather than exhaustively labeling every instance (which is labor-intensive and prone to human error, one could use active learning to have the model query a human expert for labels on only the most informative or uncertain cases [214]. Semi-supervised learning could further allow the model to learn from the abundance of unlabeled sensor data available on farms (e.g., long audio recordings) combined with the limited labeled examples. By coupling these strategies, future systems might build robust multimodal classifiers with far less manual labeling than traditionally required. In summary, expanding to a multimodal, sensor-fusion approach is promising for enhancing diagnostic accuracy and early detection of BRD. This research direction requires methodological advances in multi-sensor data fusion and pragmatic solutions for data collection and annotation on farms, but the payoff would be a more sensitive and veterinarian-like AI system that captures the full spectrum of disease indicators.

Advanced uncertainty quantification and explainability This thesis took a first step toward uncertainty-aware AI in agriculture using variational Bayesian methods. A future direction is to explore complementary or alternative approaches for uncertainty estimation that provide stronger

guarantees and interpretability. One such approach is conformal prediction, a framework that can wrap around any model to produce prediction sets with a guaranteed coverage probability [58]. Unlike Monte Carlo dropout, conformal prediction does not rely on Bayesian assumptions; instead, it uses past prediction errors to determine confidence sets for new predictions with rigorous statistical coverage (e.g., “with 90% probability, the true outcome lies in this set”). Integrating conformal prediction into our deep learning diagnostic could yield more actionable uncertainty estimates – for instance, instead of outputting a single label, the system might output a set of likely diagnoses or a range for the number of infected animals, with an associated confidence level. Matiz and Barner [209] highlighted that conformal methods can complement Bayesian neural networks by providing calibrated uncertainty measures alongside the model’s point estimates. For our hybrid model, a potential research avenue is a hybrid uncertainty approach: use Bayesian methods (like dropout) to maintain high average accuracy and sharpness of predictions, but apply conformal wrapping to ensure the uncertainty intervals are reliable (e.g., capturing the true outbreak size 95% of the time). This could result in, for example, prediction intervals for the future number of BRD cases that farmers and vets can trust to a specified probability. The practical challenge will be computational: conformal prediction typically requires an additional calibration step and may need plenty of past data for validation. Moreover, applying conformal prediction in a streaming data context (where the model is used continuously on new farms or new seasons) is an open area of research. Nonetheless, the benefit would be decision-theoretic robustness – users of the system could be presented with worst-case and best-case scenarios within a confidence bound, which might encourage more cautious and risk-aware decisions. Another aspect for future work is explainability of the model’s predictions. In high-stakes domains like animal health, users are more likely to trust and adopt AI if it can explain its reasoning. Techniques such as feature attribution (e.g., highlighting which part of an ultrasound image led to a positive diagnosis) or case-based reasoning (e.g., “this farm’s data closely resembles past outbreak X”) could be integrated so that the system not only predicts but also justifies its predictions. The Bayesian nature of our approach could be leveraged to produce explanations like “the model is only 50% confident because the inputs are unlike anything seen before,” which itself is useful information. In summary, future research should aim to enhance the trustworthiness of the hybrid model through better uncertainty quantification (possibly combining Bayesian and conformal methods) and improved explainability. This will ensure that as the model’s capabilities grow (e.g., multimodal input), its outputs remain transparent and calibrated – qualities that are essential for real-world deployment and user acceptance.

Robust simulation-based inference and model parametrisation We identified that our use of approximate Bayesian computation (ABC) for pathogen model selection is promising, but there is room to improve the efficiency and robustness of the inference. One path is to employ Sequential Monte Carlo ABC (ABC-SMC) algorithms or other advanced simulation-based inference techniques. ABC-SMC iteratively focuses simulation effort on parameter regions with higher posterior likelihood, which can greatly improve efficiency over the basic ABC rejection approach we used. By adopting an ABC-SMC approach, we could better explore complex parameter spaces, especially if we integrate more parameters or more complex mechanistic models (for example, models capturing coinfection dynamics). More robust inference could lead to finer discrimination between similar pathogen models or more precise parameter estimates for each model, thus improving the fidelity of forecasts. Additionally, recent developments like using machine learning surrogates within ABC (e.g., regression adjustments or neural density estimators) could be leveraged. For instance, replacing the simple multinomial logistic regression post-ABC with a trained classifier or using distance-learning approaches [215] might improve the power to distinguish models using high-dimensional summary data. Another consideration is joint parameter and model inference. In our work, we first identified the most likely pathogen model and then used that model’s best-fit parameters for

forecasting. A more rigorous Bayesian approach would be to treat the pathogen identity as just another parameter to infer – effectively averaging predictions over all possible models weighted by their posterior probability (a form of Bayesian model averaging). This could potentially account for uncertainty in pathogen identification in the forecasts (e.g., if two pathogens are similarly likely, the forecast might combine both possibilities). The downside is computational complexity, but ABC-SMC methods are well-suited to approximate this kind of joint inference [204]. We also note that alternative inference paradigms, like synthetic likelihood or Hamiltonian Monte Carlo for simulator-based models, are emerging and could be tested on our problem to see if they offer gains in speed or accuracy. In sum, the perspective here is to stress-test and refine the inference engine of our hybrid model. By exploring more advanced ABC variants or other likelihood-free inference techniques, future work can ensure that the model calibration and pathogen identification remain robust even as model complexity grows or as we move to more challenging datasets. Such improvements would strengthen the foundation of the entire hybrid approach, since accurate inference is critical to everything from generating trustworthy predictions to learning from new data.

Coupling to robust decision-making frameworks While we incorporated a basic economic analysis, future research can deepen the integration between epidemiological predictions and decision optimization. For example, instead of outputting a single “optimal” intervention strategy based on average outcomes, the system could use the uncertainty in its predictions to suggest strategies that are robust to worst-case scenarios. This aligns with concepts in decision theory where one seeks solutions that perform acceptably under a range of possible futures, not just the most likely future. In practice, this could mean using the posterior distribution of the mechanistic model parameters (or the predictive distribution of future cases) to evaluate interventions: e.g., choosing a treatment plan that maximizes expected profit and minimizes the risk of catastrophic loss in a bad outbreak. Techniques like Value of Information analysis could also be employed to determine if gathering more data (say, doing an extra diagnostic test) is worth the effort before making a treatment decision. Our current analysis already hinted at interventions (like selective antibiotic metaphylaxis or enhanced biosecurity) and their outcomes, but an explicit decision model would allow one to simulate policies over an entire season or production cycle. Importantly, any such decision-support extension should be evaluated not just on model outputs but on how it impacts real objectives (antibiotic use, cost, and animal welfare). Future collaboration with economists and ethicists might also consider incorporating externality costs (e.g., the societal cost of antibiotic resistance) into the decision-making objective, potentially guiding farmers towards choices that are globally optimal, not just farm-optimal. In summary, the perspective is to evolve our system from a predictive tool into a prescriptive tool – one that can recommend actions under uncertainty. Doing so will likely involve robust optimization techniques and further interdisciplinary work, but it directly addresses the end-goal of this research: not only to predict disease, but to improve disease control outcomes in practice.

Closing the diagnostic-prognostic loop with real-world trials As noted in the limitations, a critical next step is to validate and refine the integrated system through field studies and deployment pilots. One future research avenue is to implement the full pipeline – from sensor data acquisition to diagnosis to pathogen identification to recommended intervention – on a set of commercial farms, in close collaboration with veterinarians, and monitor outcomes. This would effectively test the “deep mechanistic model with pathogen-specific expert selection” in a real-world setting. Concretely, we envision using the lung ultrasound video dataset (and potentially other sensors) collected in Chapter 2 as the foundation to develop a system that, for each new batch of calves, automatically analyzes incoming sensor data, produces a probabilistic diagnosis for each calf (with uncertainty), and then uses that to infer the most likely pathogen-specific scenario via numerical solvers (e.g., ABC-SMC as

discussed). This inference could trigger specific control recommendations (for example, “outbreak likely viral – consider anti-viral and avoid antibiotics unless secondary infection signs appear”). Validation of this approach would involve biological ground truthing: for instance, collecting nasal swabs or blood samples from calves to identify the actual pathogen(s) via PCR or culture, and comparing those to the model’s inferred pathogen. Additionally, one would track metrics like antibiotic usage, illness recurrence, and weight gain in groups managed with model support versus control groups managed by standard practice. Key performance indicators would be whether the model-informed groups use significantly less medication while maintaining health and performance. Any discrepancies or failures observed during such trials would provide invaluable feedback to improve the model (e.g., if the model systematically misses a particular scenario, that model structure might need extension). We should also explore the system’s user experience during these trials: how easily can farm staff and vets interact with it? do they trust the recommendations? By iterating with user feedback, the model and interface can be adjusted (perhaps simplifying outputs or adding explanation features as discussed). Ultimately, such applied research will help transition our framework from a concept to a tangible tool. A successful field demonstration would not only prove out the efficacy of our approach but also possibly reveal new research questions (for example, how to rapidly adapt the model to a farm experiencing an atypical outbreak, or how to incorporate farmer intuition into the AI feedback loop). This “last mile” research is often where interdisciplinary projects either flourish or flounder, so careful experimental design and stakeholder engagement will be paramount. The knowledge gained from these real-world deployments will also inform any necessary regulatory approvals or guidelines for AI in veterinary practice, an emerging area that we have not yet touched but will be important for widespread adoption.

Adaptation to other domains and scalability Finally, the modular and interdisciplinary nature of our methodology lends itself to transfer and generalization to other infectious disease management problems in agriculture. Future work could test the adaptability of the hybrid model in different contexts, thereby evaluating its generality. For example, one could apply a similar deep learning + mechanistic modelling approach to swine respiratory disease in farrow-to-finish pig operations. Efforts have already been made in modelling porcine infectious diseases with multi-scale agent-based models [216], and integrating sensor data (such as cough monitors for pigs or thermal cameras for fever detection) with those models could improve early outbreak detection in swine just as we aimed to do in cattle. Another potential application is in dairy herd health monitoring beyond BRD – for instance, combining sensor-based lameness detection with a mechanistic model of disease spread in a barn to forecast and control a foot-and-mouth disease outbreak. The crop farming sector might also benefit: one could envision using imaging sensors (drones or satellites detecting crop stress) feeding into mechanistic models of pest or disease spread in fields, thereby informing integrated pest management strategies. Coupling mechanistic models in crop protection with ML that interprets sensor images of crop canopies could parallel our work in the plant domain. The challenge in transferring the methodology will lie in customizing each module to the new domain while preserving the overall architecture. The diagnostic AI would need retraining on the new sensor data, the mechanistic model would need to capture the relevant epidemiology (or pest ecology), and the economic module would change to whatever metrics matter (e.g., crop yield or market value). However, none of these require fundamentally new algorithmic development – they are matters of implementation and training, which speaks to the scalability of the approach. We anticipate that as long as the disease system has (1) some form of sensor that provides early indicators, and (2) a mechanistic understanding that can be modelled, our hybrid approach can be applied. One lesson from our work that will be valuable in other domains is the importance of modularity: keeping the components decoupled means a new team of experts can replace or modify one part (say, the pig disease model) without needing to rewrite the entire pipeline. In pursuing these new

applications, collaboration with domain experts (swine veterinarians, plant pathologists, etc.) will be crucial to ensure the models are biologically sound. Additionally, computing infrastructure and data management need to scale – a successful deployment in one sector could mean data coming from hundreds of farms, requiring robust cloud support and perhaps automated model updating as more data flows in. These are engineering challenges but foreseeable ones. In conclusion, by validating and refining our approach in other livestock or agricultural health contexts, future research can test the universality of the hybrid AI-epidemiological modelling paradigm. If successful, it would mark a significant advance in digital agriculture, providing a general blueprint for smart disease surveillance and control across different farming systems. This would amplify the impact of our initial research, contributing not only to cattle health management but broadly to the sustainability and efficiency of animal and crop health interventions in the era of precision agriculture.

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Titre : Innover pour la santé animale au travers de l'intelligence artificielle à finalité prédictible – Applications aux maladies respiratoires des jeunes bovins

Mots clés : Capteurs, Intelligence artificielle, apprentissage automatique, modèle épidémiologique mécaniste, santé animale, BRD

La gestion des maladies infectieuses en élevage nécessite de détecter et prévoir les épidémies malgré la complexité des interactions hôte-pathogène-environnement et la difficulté d'extraire des informations pertinentes à partir des capteurs en élevage. Cette thèse propose une approche innovante qui associe directement les données des capteurs à des connaissances issues de la modélisation épidémiologique mécaniste. En combinant l'apprentissage profond, capable d'extraire automatiquement des motifs dans des signaux complexes, et des modèles mécanistes reposant sur l'expertise vétérinaire, nous visons à améliorer le diagnostic à court terme et les prévisions à long terme des maladies en élevage. Les contributions principales de ce travail sont : (1) la fusion des données empiriques d'un capteur avec des simulations mécanistes, tirant parti des observations et des savoirs théoriques ;

(2) l'intégration explicite de l'incertitude dans les prédictions pour en renforcer la fiabilité ; et (3) le développement d'une méthode de différenciation des scénarios pathogéniques afin d'orienter des interventions ciblées. Appliquées aux maladies respiratoires des jeunes bovins (BRD), nos méthodes ont démontré, en conditions réelles et simulées, leur capacité à automatiser le diagnostic et à prévoir l'évolution de la maladie, ouvrant ainsi la voie à une réduction significative de l'utilisation d'antibiotiques et à une amélioration des performances des élevages. Ce travail ouvre de nouvelles perspectives en proposant une méthodologie modulaire alliant capteurs et connaissance, susceptible de constituer un outil de décision innovant pour une gestion sanitaire optimisée.

Title: Innovating for animal health through predictive artificial intelligence – Applications to respiratory diseases in young cattle.

Keywords: Sensors, artificial intelligence, deep learning, epidemiological mechanistic modelling , animal health, BRD

Effective management of infectious diseases in livestock requires detecting and forecasting outbreaks despite the complexity of host-pathogen-environment interactions and the difficulty of extracting relevant information from farm sensors. This thesis proposes an innovative approach that directly couples sensor data with knowledge derived from mechanistic epidemiological modeling. By combining deep learning, which can automatically extract patterns from complex signals, with mechanistic models based on veterinary expertise, we aim to improve both short-term diagnosis and long-term disease predictions in livestock. The main contributions of this work are: (1) coupling empirical sensor data with mechanistic simulations to fill the gap between sensor-based observations and theoretical knowledge;

(2) explicitly incorporating uncertainty into predictions to enhance reliability; and (3) developing a method to differentiate pathogen-specific scenarios to guide targeted interventions. Applied to respiratory diseases in young cattle (BRD), our methods have demonstrated, under both real and simulated conditions, their ability to automate short-term diagnosis and long-term predictions BRD dynamics, thereby significantly reducing antibiotic use and improving farm performance. This work opens new perspectives by proposing a modular methodology that combines sensor data and knowledge, potentially serving as an innovative decision-support tool for optimized health management.

