

PhD project: Precision phenotyping for genetic improvement of disease resistance and resilience, with focus on mastitis in cattle - a modelling approach

In short

This PhD proposes to develop new health traits that reflect individuals' genetic capacity for resistance and resilience in the face of infection, with a view to improved genetic selection. The development of new health traits will be carried out using dynamic models applied to high-frequency health and performance time-series data. The central challenge of this project is to capture the dynamic and continuous nature of an individual's health status relative to disease events, and accounting for the recurrence of such events. With a strong genetic focus, this thesis will offer new perspectives on selection to facilitate the transition toward more sustainable and agroecological livestock production.

Applicants should send a CV and letter of motivation to:

Pauline.martin@inrae.fr ; Nicolas.friggens@inrae.fr ; Rafael.Munoz-Tamayo@inrae.fr

Presentation of INRAE, the PhD working environment

The National Research Institute for Agriculture, Food, and the Environment (INRAE) is a public research institution comprising a workforce of 12,000 people, with 272 research, service, and experimental units located in 18 centres throughout France. INRAE ranks among the world's leading institutions in agricultural and food sciences, as well as plant and animal sciences. Its research aims to develop solutions for high-performance agriculture, high-quality food, and the sustainable management of resources and ecosystems

This PhD position will be based at the Animal Genetics and Integrative Biology Unit (GABI - <https://gabi.jouy.hub.inrae.fr/>), within the Genetics for the Sustainability of Cattle Farming (GBOS) team, at the INRAE site in Jouy-en-Josas (78). It will be carried out in close collaboration with the units: Systemic Modeling Applied to Ruminants (MoSAR - <https://mosar.versailles-saclay.hub.inrae.fr/>), and Physiology, Environment, and Genetics for Animals and Livestock Systems (PEGASE - <https://pegase.rennes.hub.inrae.fr/>).

Context and Research Questions

Health data from farm animals is generally viewed and recorded in binary terms: the animal is either healthy or sick with respect to a given condition at a given time. This approach to phenotyping health status leaves no room for nuance, and it seems likely that a more detailed description of the variability in animals' responses would be useful for genetic selection of disease resistance. In recent years, the deployment of sensors and high-throughput technologies in a growing number of farms has provided access to time-series of numerous automated measurements at the animal level (Delaval OCC, Herd Navigator, O-CMT, etc.) (Sørensen et al., 2016; Deng et al., 2020). These data open up the possibility of tracking the evolution of health indicators over time. Better integration of the dynamic dimension of health status into a quantitative measure would constitute a real advance in phenotyping, but also presents a methodological challenge regarding the extraction of biologically relevant indicators from such longitudinal measurements.

A few studies have already begun to explore this question (e.g., Detilleux et al., 2006), and recently, a model representing the degree of infection as a continuous trait during a health disturbance and incorporating an animal-specific genetic component was proposed by the researchers supervising this thesis. The model describes the change over time in the degree of infection (DOI) using three coefficients that account for individual variations among animals in terms of their ability to clear the infection, i.e., their resistance. Furthermore, by incorporating changes in performance over time (e.g., milk production), the model also describes the effect of infection on performance, thereby allowing for the estimation of individual variation in resilience to infection.

The proposed modelling approach is based on biological principles similar to those used by Detilleux and colleagues. However, instead of applying them in an epidemiological context (modelling disease transmission within a herd), it is here designed to enable the extraction of genetic parameters related to the response to the disease. To our knowledge, this is the first model of its kind intended for use in a genetic context. As part of a proof-of-concept study, the preliminary model was evaluated using 15 individual time series of somatic cell counts in milk associated with episodes of mastitis, and the results are promising. Following this initial step, however, the model still needs to be adapted for use on large datasets and its performance evaluated across a wider range of farming systems and data sources. Furthermore, the model's structure is designed to facilitate the estimation of animal parameters using statistical tools for dynamic modelling. This extension would provide the appropriate statistical framework for addressing measurement uncertainty, an aspect that has not yet been addressed. Another key aspect to evaluate concerns the issue of repeated infections during the same lactation. Should they be considered as related but genetically distinct, or as repeated measurements of the same underlying trait?

In this PhD, you will conduct research at the intersection of genetics and modelling to address the following questions:

- Do phenotypes derived from mechanistic models of disease resistance or resilience provide a level of precision that is both meaningful and practical for health-based selection compared to current traits?
- Are genetic differences in resistance and resilience observed when comparing different pathogens, or between repeated infections.

To address such questions you will use the pseudo-phenotypes derived from the model, whose underlying principles are described in the article "Phenotyping health status on a continuous scale using a degree of infection approach: a case study using mastitis" (Martin et al., under review). You will be required to adapt this model to make it better suited for large-scale data, and will also need to develop new modules to account for the recurrence of events experienced by the animals. Finally, you

will use classical methods of quantitative genetics (estimation of genetic parameters, GWAS and post-GWAS analyses) to test the suitability of your pseudo-phenotypes for use in breeding. Depending on the progress of the thesis, a pilot evaluation of the selected traits may also be conducted.

Various types of data will be made available to you:

- data from the Le Pin experimental unit (<https://uep.isc.inrae.fr/>), which contains several thousand lactations with biweekly somatic cell counts, including approximately 200 lactations in which the pathogens causing mastitis have been identified. This data continues to grow as part of the ongoing GLOBAL experiment, with cell counts now performed three times a week and pathogen identification now conducted systematically. This new experiment also provides extensive knowledge about the animals, particularly regarding numerous blood parameters related to immunity.
- large-scale data from commercial farms equipped with milking robots and provided by the French dairy industry. International data could also be shared as part of this thesis.

Education and Required Skills

A Master's degree or equivalent (5 years of higher education) is required. A background in animal science, genetics, or mathematical modelling is strongly recommended.

Highly motivated by science, you should demonstrate independence, curiosity, rigor, and a genuine sense of initiative. Fluency in English is required; knowledge of French is optional.

References

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Sørensen, L.P., Bjerring, M., Løvendahl, P., 2016. Monitoring individual cow udder health in automated milking systems using online somatic cell counts. *Journal of Dairy Science* 99, 608–620. doi:10.3168/jds.2014-8823

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