Advancing global health through an innovative approach for tick-borne disease surveillance and control: MALDI-TOF mass spectrometry coupled with artificial intelligence

Introduction

Tick-borne diseases are a growing global health concern in Europe and worldwide. **Climate change** and **environmental shifts** are accelerating the **geographical expansion of ticks**, highlighting the need for a better understanding of the factors influencing tick survival and tick-borne pathogen transmission. People are exposed to potentially infected tick-bites for longer periods of time each year, and they need to be aware of these changing risk patterns where they live and travel. In Europe, hard ticks of the genus *Ixodes*, particularly *Ixodes ricinus*, are the primary vectors of **Lyme borreliosis** and **tick-borne encephalitis**, both posing significant public health risks. Despite their public health importance, **tools to study their epidemiology remain limited** and the development of new control strategies is hampered by a lack of understanding of tick biology and tick-pathogen-host interactions. Thus, there is an urgent need for operationally attractive entomological tools that can quantify tick ecology with precision, improve epidemiological surveillance, increase public awareness, and inform targeted prevention strategies to protect populations.

MALDI-TOF mass spectrometry is a widely used tool in clinical microbiology and has already demonstrated its potential for identifying arthropod species of medical interest, including ticks (1, 2). Studies have also shown that MALDI-TOF can also differentiate tick developmental stages (larva, nymph, adult) based on protein profiles (3). This technique is fast, robust and inexpensive, and new MALDI-TOF instruments can now produce both protein and lipid profiles, expanding its potential applications. Beyond species identification, **recent pioneering studies** by members of this project have shown that **MALDI-TOF, combined with artificial intelligence algorithms**, **can predict key malaria transmission determinants** such as *Anopheles* mosquito age, blood meal history and *Plasmodium* infection, from an insectarium colony (4). Notably, the age prediction in mosquitoes was field-validated, achieving a **high precision** of ±2 days (5). The success of this approach suggests that **there is great untapped potential for the characterization of ticks' biology by the application of the same approach.**

Objective of the project

This project aims to provide new entomological tools for **tick-borne disease surveillance and control** using an **innovative multidisciplinary approach** combining MALDI-TOF mass spectrometry and artificial intelligence. We hypothesize that this approach can be used to estimate key biological parameters, such as tick age and the host of the last blood meal, providing crucial insights into tick population dynamics and pathogen transmission determinants**.** By bridging **Ecology, Public Health and Digital Health** we seek to **advance epidemiological modelling** and **contribute to strengthen global efforts to control these diseases**, ultimately mitigating their impact on human and animal health. This research builds on several years of expertise developed by our consortium in mass spectrometry data analysis using artificial intelligence (6). We have already evaluated state-of-the-art neural network architectures, including one- and two-dimensional convolutional neural networks, recurrent neural networks and autoencoders, integrated with various spectral representations. These models have demonstrated their effectiveness in advancing MALDI-TOF applications by classifying spectra and detecting fine intensity variations in mass spectra.

Methodology and milestones

The proposed PhD work involves the analysis by MALDI-TOF mass spectrometry, biomarker identification, and application of deep learning to predict tick biological parameters, from ticks produced or provided by the members of this project. More specifically**, to assess age-related changes**, healthy (uninfected) ***Ixodes*** **ticks are blood-fed on rabbits** at the larval and nymphal stages at the ANSES laboratory (Sara MOUTAILLER, Maisons-Alfort, UMR BIPAR, Jun 2024 - Dec 2025). Engorged ticks are incubated (18-22°C, 90-95% relative humidity) to facilitate molting to the next stages. A subsample of ticks is retained for analysis at age day 0 (end of engorgement) and then monthly post-metamorphosis for up to 12 months. As of February 2025, 260 ticks are already available, and a total of **about 600 ticks are expected**. In a second phase, **ticks engorged on known wild hosts** will also be analyzed to identify host-specific biomarkers for blood meal sources other than rabbits (samples already collected, provided by Olivier PLANTARD, INRAE, UMR BIOEPAR, Nantes); and **ticks collected in the wild in France and Romania** will be used for validation (Serban MOROSAN, UMS28, Sorbonne University, Ion Ionescu de la Brad University of Iasi, Romania).

The main steps of the PhD project are to:

(1) **Conduct a systematic literature review** to better understand the ecology of *Ixodes* ticks and the entomological tools available to characterize them and their determinants of pathogen transmission, with a focus on vector control and global health perspectives;

(2) **Acquire MALDI-TOF mass spectra and perform protein and lipid profiling**: the candidate will acquire mass spectra data using two MALDI-TOF instruments available for research use at the Pitié-Salpêtrière Hospital: Bruker MALDI Biotyper Microflex LT for protein profiling (Parasitology-Mycology Department) and Bruker MALDI Biotyper Sirius for lipid profiling (Bacteriology Department); the candidate will then visualize the spectral data to ensure data quality and identify discriminating biomarkers with significant difference in peak intensity by protein and lipid profiling using PCA (Principal Component Analysis) and t-test ANOVA;

(3) **Analyze mass spectra using deep learning algorithms**: the candidate will collaborate with computer scientists at the laboratory of medical informatics of the Sorbonne University (Prof. Xavier TANNIER's team, Sorbonne University, LIMICS, Paris) to analyze spectral data as input for deep learning models to predict biological parameters of ticks. Different models (Convolutional Neural Networks, Recurrent Neural Networks and Autoencoders) and prediction methods (classification and regression) will be tested to optimize performance;
(4) **Disseminate the results**: the PhD project should result in at least two scientific peer-reviewed publications and one or more presentations at international conferences such as the European Society for Vector Ecology (ESOVE) or the World One Health Congress. A first publication is expected in mid-thesis: "Predicting the age and blood meal host of *Ixodes* ticks using mass spectrometry and artificial intelligence: implications for tick-borne disease surveillance".

Impact and benefits

Interdisciplinarity to develop cutting-edge entomological tools

By gathering the **complementarity of disciplines that are rarely combined** such as medical entomology, proteomics, lipidomics, bioinformatics, and infectious disease modeling, **this project pioneers a transformative approach to tick-borne disease research,** combining MALDI-TOF and artificial intelligence for the first time to study tick ecology. The project's interdisciplinary co-directorship, with an **entomologist/medical biologist** (Dr. Cécile NABET, MCU-PH, Sorbonne University, IPLESP), an **infectious disease modeler/public health specialist** with expertise in tick-borne diseases modelling (Dr. Raphaëlle METRAS, Inserm researcher, IPLESP), and a **specialist in machine learning** (Prof. Xavier TANNIER**,** LIMICS, Sorbonne University) ensures that our results will have broad implications for both basic science and applied vector-borne disease control. Furthermore, the experience gained in spectral data analysis positions our consortium as a **leader in MALDI-TOF mass spectra analysis using artificial neural networks**.

Global health benefits and disease prevention

This project **addresses critical gaps in tick-borne disease prevention** by developing **innovative surveillance tools** to improve vector management. In the short term, it will improve our understanding of tick survival or host-vector interactions, while developing an **online application** for **real-time monitoring of tick populations by health professionals and researchers** (already developed at Sorbonne University & APHP, MSI). By refining pathogen transmission models, our findings will improve **risk assessment** and inform **targeted public health policies,** thereby reducing health disparities in tick-borne diseases (7, 8). In the long term, **extending the tool to pathogen detection in ticks (**beyond this proof-of-concept on healthy ticks) could further transform tick surveillance, enabling **pathogen detection** from ticks, collected by the community or researchers, for **better risk assessment**. By providing AI-based surveillance tools to improve epidemiological monitoring of tick populations, this approach could provide **early warning systems** for tick-borne diseases such as Lyme disease and tick-borne encephalitis, contributing to more effective prevention measures and targeted vector control programs in endemic and emerging areas.

International collaboration with Romania

A key component of this project is an international partnership with Ion Ionescu de la Brad University of Iasi (Veterinary faculty) in Romania, where tick-borne diseases are an emerging public health concern. Collaboration with Dr MOROSAN and colleagues will facilitate field studies and validation across diverse ecological settings, enhancing the **generalizability of findings**. This partnership also **promotes knowledge exchange**, **capacity building** and joint efforts in vector control strategies, strengthening tick surveillance and understanding of the epidemiology of tick-borne diseases in Europe and beyond.

Conclusion

This project has the potential to transform tick surveillance, offering a shift in how we monitor, predict, and control tick-borne diseases in an era of accelerating global change. By combining **MALDI-TOF mass spectrometry and artificial intelligence**, this research seeks to refine pathogen transmission models and provide **real-time monitoring tools, benefiting both the community and public health professionals**. The collaboration with Romania strengthens international partnerships and knowledge exchange in tick-borne disease research. By improving **public awareness** and **informing public health policies**, this project could **have a significant impact on global health** by **improving tick-borne disease surveillance and prevention strategies.**

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