The challenge is to analyze these BIG DATA to answer clinical and biological questions by using appropriate statistical methods. With data on the machinery of a cell to the clinical status of individuals in any circumstances including in clinical trials, new tools are needed to translate information obtained from complex systems into knowledge. This has led to the field of « systems biology » and « systems medicine » by extension, which naturally takes place in the context of translational medicine that links clinical and biological research. The statistical analysis of these data is facing several issues:

- There are more parameters (p) to estimate than individuals (n)
- The types/nature of data are various
- The relationship between variables is often complex (e.g. non linear) and can change over time to tackle these issues we are developing specific approaches for these questions, often related to immunology.

The methods are mainly based on either mechanistic modeling using differential equation systems or on statistical learning methods. The general paradigm of our approach is to include as much information as available to answer a given question. This information comes from the available data but also from prior biological information available defining the structure of the model or restricting the space of the parameter values. We develop and apply our methods mainly for applications belonging to clinical research especially HIV immunology.

For instance, several projects are devoted to the modelling of the response to antiretroviral treatments, immune interventions or vaccine in HIV infected patients. Applications are provided by the Vaccine Research Institute (VRI), other teams in the research centre and the Bordeaux Hospital Clinical Trial Unit (CTU).

Contexte et atouts du poste

Infectious diseases, and especially the last COVID-19 pandemics, have important impact on our societies in term of public health, social and economic issues. To mitigate this impact, significant understanding of the dynamics of spreading of such diseases, associated to methods enabling to optimize and quantify the impact of intervention strategies and their uncertainties, are key to inform policy making. For example, in the COVID-19 context, major decisions to confine the population at large scale were made based on analysis and predictions of mathematical models (Ferguson et al., 2005, 2006, 2020; Cauchemez et al., 2019). In this process, the method has used to be consider a few relatively coarse pre-defined intervention strategies (such as isolation or not) and run predictions of their impact on the epidemics dynamics on mathematical models of epidemic spread (Ferguson et al., 2020). However, given the complexity of the epidemic dynamics (and the associated complexity of models), these pre-defined coarse strategies are bound to be sub-optimal, especially when considering that the problem is multi-objective (e.g. ranging from public health objectives related to number of deaths and ICU saturation to societal and economic objectives) and that strategies may be heterogeneous and multiscale (Halpern et al., 2008).

Mission confiée

The hypothesis we make in this project is that more sophisticated and adaptive strategies could be more efficient, and finding them involves using advanced optimization methods over different kinds of epidemic models. More precisely, we aim to study and adapt the use of state-of-the-art deep reinforcement learning methods which have been shown in other domains to enable find efficient and robust action policies in high-dimensional non-stationary environments with uncertainty and partial observation of the state of the system (Mnih et al., 2015; Haarnoja et al., 2018).

In a first phase of the project, one will compare and select one representative model of epidemic dynamics of the COVID-19 in each of the two following families:

1. Macroscopic mechanistic models based on ordinary differential equations (or their stochastic counterparts), which are useful when one has only access to aggregated surveillance data at the level of large geographical areas. For this, we will build on and reuse ongoing work on developing such a model in the SISTM Inria team, related to a recent model presented in (Wang et al., 2020), and using maximum likelihood techniques based on Stochastic Approximation Expectation Maximization algorithm to estimate the parameters of the model.
2. Individo-centered mechanistic models (also called multi-agent models) that take into account more fine-grained information such as the structure of social and spatial networks in the population (Salje et al., 2016), and used recently to inform emergency decision of isolation for the COVID-19 pandemics (Ferguson et al., 2020).

In a second phase, one will focus on studying the optimization of centralized global intervention strategies by using deep reinforcement learning systems (i.e. strategies applied uniformly at the scale of a large geographical area, with few parameters). In particular variants of these algorithms that enable to deal with complex time-dependent dynamics and partial observability (thus we will consider in particular approaches using recurrent neural networks or attention-based architectures). Since models of the epidemic dynamics are available, we will consider model-based deep reinforcement learning approaches (e.g. Chua et al., 2018; Wang et al., 2019), and compare them with model-free approaches (e.g. Mnih et al., 2015; Haarnoja et al., 2018) as well as with more traditional optimization techniques ranging from black-box stochastic optimization to model-based predictive control. The robustness and interpretability of the solutions will be of particular importance in the
In a third phase, one will study the optimization of heterogeneous multi-scale decentralized intervention strategies (e.g., different mitigation actions in different places for different categories of people) using deep multi-agent reinforcement learning algorithms (with centralized learning and decentralized action, Lowe et al., 2017; Rashid et al., 2020). These will be tested by focusing on multi-agent models or variants of ODE models that are spatialized and incorporate finer-grained compartments.

References


Principales activités

The scientific outcome of this project will aim to be published in wide audience interdisciplinary journals (e.g. PNAS, Nature Communication/Methods) as well as in specialized venues in epidemiology (introducing the community to deep reinforcement learning tools) and machine learning (raising the interest of this community for this societally important application area).

The project will be co-supervised by Mélanie Prague (SISTM research group [1]) and Clément Moulin-Frier (FLOWERS research group [2]), benefitting from the expertise of SISTM in methods for modeling phenomena associated to infectious diseases and their evaluation (e.g. Prague et al. 2012, Villain et al. 2019, Pasin et al. 2019), and from the expertise of FLOWERS in deep reinforcement learning and multi-
agent deep reinforcement learning (e.g. Colas et al., 2018, 2019, 2020).


Compétences

Prior experience with Deep Reinforcement Learning is required.
Technical skills and level required: Excellent programming skills in Python, with experience with Pytorch or Tensorflow. Experience with R is a plus.
Languages: Fluent in oral and written English.

See also section "The keys to success"

Avantages

- Subsidized meals
- Partial reimbursement of public transport costs
- Possibility of teleworking (after 6 months of employment) and flexible organization of working hours
- Professional equipment available (videoconferencing, loan of computer equipment, etc.)
- Social, cultural and sports events and activities
- Access to vocational training
- Social security coverage

Rémunération

2653€ / month (before tax)