Main activities

We propose to combine exploratory analysis, dimension reduction methods for high dimensional data, mathematical dynamical modeling and optimal control theory to answer these questions.

Assignment

We propose to combine exploratory analysis, dimension reduction methods for high dimensional data, mathematical dynamical modeling and optimal control theory to answer these questions.

General Information

- **Theme/Domain**: Modeling and Control for Life Sciences
- **Town/city**: Talence
- **Inria Center**: CRI Bordeaux - Sud-Ouest
- **Starting date**: 2018-10-01
- **Duration of contract**: 3 years
- **Deadline to apply**: 2018-05-24

Contacts

- **Inria Team**: SISTM
- **Recruiter**: Prague Melanie / melanie.prague@inria.fr

Conditions for application

- **Advisors**: Rodolphe Thiébaut (HDR) & Mélanie Prague

Thank you to send:

- Copy of master thesis diploma
- Master marks and ranking
- 2 pages CV
- Cover letter
- Support letter(s)

Defence Security:
This position is likely to be situated in a restricted area (ZRR), as defined in Decree No. 2011-1425 relating to the protection of national scientific and technical potential (PPST). Authorisation to enter an area is granted by the director of the unit, following a favourable Ministerial decision, as defined in the decree of 3 July 2012 relating to the PPST. An unfavourable Ministerial decision in respect of a position situated in a ZRR would result in the cancellation of the appointment.

Recruitment Policy:
As part of its diversity policy, all Inria positions are accessible to people with disabilities.

**Warning**: you must enter your e-mail address in order to save your application to Inria. Applications must be submitted online on the Inria website. Processing of applications sent from other channels is not guaranteed.
Based on this general objective description, we expect to organize the work in three different tasks:

1/ Develop methods for integration and exploitation of heterogeneous data acquired on a patient and on a population. We will assimilate data from multiple sources using lasso-type methods to further understand what can be seen as a correlate of efficacy. In particular, we will be interested in identification and validation of an early correlate of late antibody response. It would allow early prediction of whether an individual, or group of individuals is likely to be a good or poor immunological responder [5]. Methods based on joint non-linear mixed models and sparse PCA will be investigated.

2/ Extend existing methods to estimate parameters in mechanistic models by using assimilation approaches based on filtering methods and compare them with penalized maximum likelihood as implemented in NIMROD [4]. In particular, we believe that these filter methods, which jointly estimate state and parameters, can help addressing the fact that biomarkers can sometimes not be observed but are only deduced from surrogate information. A particular example lies in gene expression information which may carry cells count information if proper deconvolution is used.

3/ Develop an optimal protocol to individualize and optimally choose a vaccination strategy using machine learning and particularly neural network approaches. The idea is that it is possible to build synthetic data with annotated optimal choice from the mechanistic model by using computer based simulation and that these datasets can be used as learning examples for neural network approaches. We will compare this approach with existing approaches developed in the team such as Bayesian predictions and dynamic programming based on Markov impulse theory.

These methods will be illustrated on available clinical data, and particularly on the EBL1001+EBL1003+EBL1004 and VR101 trials described in the previous section for which we have measurement of humoral response, cellular response and transcriptomic data in respectively 216 and 92 individuals. More than eight longitudinal follow-up guaranty good quantity of dynamic information. Moreover, these studies enable us to investigate the same viral vector (MVA) for different infectious diseases. We expect to publish the results in journals both theoretical and more applied to clinical practices. Finally, we expect that a software for joint analysis of multiple sources data in immunological studies will be developed and disseminated.

**Keywords**: Applied mathematics, Simulation and calculus, Biostatistics, Mixed effects dynamical models, control theory, vaccination

**References**:


**Skills**

**Required Knowledge and background**: We seek for a very good master-level student (possibly from a French engineer school or foreign universities) with strong background in mathematics and/or statistics. We request good programming skills in any language, and a good knowledge of R. Proficient written and spoken English is needed. Previous experience in research, possibly working with differential equations or immunology, will be seen as a very competitive advantage.

**Benefits package**

- Subsidised catering service
- Partially-reimbursed public transport

**Remuneration**

1982€ / month (before tax) during the first 2 years, 2085€ / month (before tax) during the third year