Offer #2021-04259

Post-Doctoral Research Visit F/M Post-doctoral research fellowship OR research scientist in modelling of the immune response to vaccine

Contract type : Fixed-term contract

Renewable contract : Yes

Level of qualifications required : PhD or equivalent

Fonction : Post-Doctoral Research Visit

About the research centre or Inria department

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 mecanistic 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).

Context

One postdoc position (post PhD degree) OR one engineer position (post Master2 degree) is available to work on the modelling of the immune response to Nipah vaccine and antiviral therapies at Inserm U1219 Bordeaux Population Health Center, Statistics in Systems and Translational Medicine team (SISTM) in Bordeaux (France) for a minimum period of 12 months.

Nipah virus (NiV) is a recently emergent, highly pathogenic, zoonotic paramyxovirus first recognized following a 1998-99 outbreak of severe febrile encephalitis in Malaysia and Singapore (Chua et al., 2000). NiV can cause atypical pneumonia or necrotizing alveolitis with hemorrhage, pulmonary edema and aspiration pneumonia, leading to acute respiratory distress syndrome. As for the huge majority of risk group 4 pathogens, the knowledges on NiV virus infection remain very limited. Diagnosis, therapeutic and prophylactic means still
do not exist. The Nipah project funded by the « Ministere de l'enseignement supérieur, de la recherche et de l'innovation » investigates these aspects in collaboration with Chinese institutions.
In this project, the SISTM team directed by Pr. Rodolphe Thiébaut aims at conducting the analysis and the modelling of the immune response to antiviral and vaccine strategies, using the data produced in pre-clinical and Phase I clinical, including immunological sub studies recording many biomarkers (cell phenotype, functionality, gene expression, antibody titers...).

SISTM is a team belonging to INSERM U1219 Bordeaux Population Health and INRIA Bordeaux Sud-Ouest research institutes. The group is dedicated to the analysis and the modelling of the data generated in epidemiology and medicine with a special focus on vaccines and immune interventions in HIV and other infectious diseases. Its expertise is mainly in biostatistics with a special emphasis on dynamical models based

on ODE and statistical learning using moderately high dimensional data.

Assignment

As the SARS-CoV-2 crisis delayed almost all experiments for the Nipah project, the main objective of this postdoc position will focus on methods developments. Application of these methods to real datasets will also be possible thanks to Ebola projects (EBOVAC series) and Sars-CoV-2 projects (EMERGEN).
Model building is a crucial problem when modeling data using mechanistic models (see an example in Pasin et al. 2019). The mathematical model based on ordinary differential equations must be chosen and its identifiability must be verified. Then, a statistical model must be built on the parameters of the modelto understand the link between 1/ the available descriptive variables and parameters 2/ the residual variability due to the heterogeneity of the observed individuals. Finally, the observation model allowing to link the data
to the trajectories of the model need to be specified. Most of the model building strategy rely on the optimization of a penalized log-likelihood.

Main activities

We propose to build strategies around these topics including covariate model building, selecting the best penalization this covariate model building and down selecting parameters on which random effects are mandatory to model the inter-individual variability, Estimation will be based on likelihood optimization based on the SAEM algorithm as implemented in lixoft Monolix suite. All
development will be made in R. Part of this work will be done in collaboration with Marc Lavielle from Inria Saclay Xpop at Ecole Polytechnique.
Other integrative analysis such as exploratory analysis may also be achieved on the data generated in the Nipah project. In particular, Principal component analysis (PCA) which is a technique for reducing the dimensionality of large datasets, increasing interpretability but at the same time minimizing information loss. Part of this work will be done in collaboration with Jérémie Guedj from Inserm IAME, Université de Paris.
The candidate will be integrated in a team of biostatisticians and modelers working on related topics: modeling of HIV vaccine response. The candidate will benefit from a very attractive environment with computing facilities and close collaborations with mathematicians (from INRIA and INSERM research centers) and immunologists (from the Labex Vaccine Research Institute).

Skills

The candidate should hold a PhD (or at least M2 degree) in mathematics, physics or statistics. We are looking for a highly motivated candidate with an outstanding potential and a strong background in statistics and a deep interest in immunology and biological application. Proven experience in R language is required. The ideal candidates are able to work effectively as part of a team, but also to develop and pursue independent ideas. The successful candidates are expected to conduct innovative research at the highest international level.
Experience in biostatistics and computational biology is highly recommended. Previous work in immunology/Vaccinology, systems biology will be highly appreciated but not mandatory.
The expected starting date can be as soon as possible. Salary will follow Inserm rates and can be negotiated to be higher depending on previous experience and skills

Benefits package

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

Remuneration

2653€ / month (before taxs)

General Information

- **Theme/Domain :** Optimization, machine learning and statistical methods
  Data production, processing, analysis (BAP D)
- **Town/city :** Talence
- **Inria Center :** Centre Inria de l'université de Bordeaux
- **Starting date :** 2022-01-01
- **Duration of contract :** 12 months
- **Deadline to apply :** 2022-06-01

Contacts

- **Inria Team :** SISTM

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

About Inria

Inria is the French national research institute dedicated to digital science and technology. It employs 2,600 people. Its 200 agile project teams, generally run jointly with academic partners, include more than 3,500 scientists and engineers working to meet the challenges of digital technology, often at the interface with other disciplines. The Institute also employs numerous talents in over forty different professions. 900 research support staff contribute to the preparation and development of scientific and entrepreneurial projects that have a worldwide impact.

The keys to success

There you can provide a "broad outline" of the collaborator you are looking for what you consider to be necessary and sufficient, and which may combine :

- tastes and appetencies,
- area of excellence,
- personality or character traits,
- cross-disciplinary knowledge and expertise...

This section enables the more formal list of skills to be completed and 'lightened' (reduced) :

- "Essential qualities in order to fulfil this assignment are feeling at ease in an environment of scientific dynamics and wanting to learn and listen."
- " Passionate about innovation, with expertise in Ruby on Rails development and strong influencing skills. A thesis in the field of **** is a real asset."

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.

Instruction to apply

Thank you to send:

- CV
- Cover letter
- Support letter (mandatory)
- Diploma thesis
- List of publication

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.