Offre n°2020-02798

PhD Position F/M Mathematical modeling and prediction of clinical metastatic relapse

Le descriptif de l'offre ci-dessous est en Anglais

Niveau de diplôme exigé : Bac + 5 ou équivalent

Fonction : Doctorant

A propos du centre ou de la direction fonctionnelle

The Inria Sophia Antipolis - Méditerranée center counts 34 research teams as well as 8 support departments. The center's staff (about 500 people including 320 Inria employees) is made up of scientists of different nationalities (250 foreigners of 50 nationalities), engineers, technicians and administrative staff. 1/3 of the staff are civil servants, the others are contractual agents. The majority of the center's research teams are located in Sophia Antipolis and Nice in the Alpes-Maritimes. Four teams are based in Montpellier and two teams are hosted in Bologna in Italy and Athens. The Center is a founding member of Université Côte d'Azur and partner of the I-site MUSE supported by the University of Montpellier.

Contexte et atouts du poste

The PhD project will take place in the environment of the new Inria-Inserm team COMPO (COMputational Pharmacology in Oncology), located in the pharmacy faculty of the University Hospital of Marseille. This team is composed of mathematicians, pharmacists and clinicians and is a unique multidisciplinary environment focused on developing novel computational tools for decision-making in clinical oncology.

Mission confiée

Project aims
This PhD subject aims at establishing and validating on clinical data mathematical, mecha- nistic models of metastatic apparition and development in cancer patients, by using statis- tical (machine) learning methods applied to clinical data sets.

Description of the project

Background
Metastasis and associated complications are the cause of 90% of deaths from cancer. In breast cancer for instance, determining the extent of the residual metastatic disease following surgery is a major clinical challenge in order to personalize the adjuvant treatment. Nowadays, on top of classical demographic variables, several biological and molecular biomarkers predic- tive of metastatic relapse are measurable at diagnosis, including genetic expression signatures [van 't Veer et al., 2002]. So far, these parameters have been included into survival statistical models but no mechanistic, biologically grounded mathematical model of metastasis has been validated on large data sets.

Methodology
Based on previous work of mathematical modeling of metastatic development validated on pre- clinical data [Benzekry et al., 2016] and more recently on clinical data [Nicolo et al., 2020], the primary step will be to improve existing models of metastatic dynamics based on the biological mechanisms. Briefly, the model consists in a partial differential equation of transport type for description of a population of tumors, which depends on several patient-specific parameters for simulation of the metastatic development. Modeling of the effect of post-surgery therapy will also be developed in collaboration with oncologists and radiotherapists. The different tasks will be:

- To refine previous work in relation to existing molecular classifications of breast cancer
- To include dormancy in the breast cancer model
- To extend previous results to new datasets
- To study the use of deep learning algorithms for prediction of metastasis-free survival from high-throughput data
- To include and validate the effect of adjuvant therapy in the model

In order to do so, the intern will work on clinical data sets from collaborations with clinical oncologists.

These include databases of: breast cancer (with respectively n=1057 and n=174 patients), lung cancer (n=350 patients) neuroblastoma (n=48 patients) and melanoma (n=212).

In addition, use of machine and deep learning algorithms from publicly available high-throughput data (genomics and imaging) will be investigated and combined with the previous mathematical model.

[Benzekry et al., 2016] Benzekry, S., Tracz, A., Mastri, M., Corbelli, R., Barbolosi, D., and Ebos, J. M. L. (2016). Modeling Spontaneous Metastasis following Surgery: An In Vivo-In Silico Approach. Cancer Res, 76(3):535–547.

[Nicolo et al., 2020] Nicol`o, C., Perier, C., Prague, M., Bellera, C., MacGrogan, G., Saut, O., and Benzekry, S. (2020). Machine learning and mechanistic modeling for prediction of metastatic relapse in early-stage breast cancer. JCO: Clinical Cancer Informatics, 4(4), 259–274.

[van 't Veer et al., 2002] van 't Veer, L. J., Dai, H., van de Vijver, M. J., He, Y. D., Hart, A. A. M., Mao, M., Peterse, H. L., van der Kooy, K., Marton, M. J., Witteveen, A. T., Schreiber, G. J., Kerkhoven, R. M., Roberts, C., Linsley, P. S., Bernards, R., and Friend, S. H. (2002). Gene expression profiling predicts clinical outcome of breast cancer. Nature, 415(6871):530–536.

Keywords

Mechanistic modeling; metastasis; artificial intelligence; cancer

Principales activités

Main activities (5 maximum) :

- Reading biological and clinical literature
- Statistical data analysis
- Mathematical (mechanistic) modeling
- Programming

Compétences

Required skills

- Master of science in either applied mathematics, statistics, bioinformatics or theoretical physics.
- Good programming level in either python (preferred), R or matlab
- Good oral and written communication skills in English

Avantages

- Subsidized meals
- Partial reimbursement of public transport costs
- Leave: 7 weeks of annual leave + 10 extra days off due to RTT (statutory reduction in working hours) + possibility of exceptional leave (sick children, moving home, etc.)
- 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

Duration: 36 months
Location: Sophia Antipolis, France
Gross Salary per month: 1982€brut per month (year 1 & 2) and 2085€ brut/month (year 3)

Informations générales

- **Ville :** Marseille
- **Centre Inria :** Centre Inria d'Université Côte d'Azur
- **Date de prise de fonction souhaitée :** 2020-11-02
- **Durée de contrat :** 3 ans
- **Date limite pour postuler :** 2020-10-30

Contacts

- **Équipe Inria :** DIR-SOP
- **Directeur de thèse :**
  Benzekry Sebastien / Sebastien.Benzekry@inria.fr

A propos d'Inria

Inria est l'institut national de recherche dédié aux sciences et technologies du numérique. Il emploie 2600 personnes. Ses 215 équipes-projets agiles, en général communes avec des partenaires académiques, impliquent plus de 3900 scientifiques pour relever les défis du numérique, souvent à l'interface d'autres disciplines. L'institut fait appel à de nombreux talents dans plus d'une quarantaine de métiers différents. 900 personnels d'appui à la recherche et à l'innovation contribuent à faire émerger et grandir des projets scientifiques ou entrepreneuriaux qui impactent le monde. Inria travaille avec de nombreuses entreprises et a accompagné la création de plus de 200 start-up. L'institut s'efforce ainsi de répondre aux enjeux de la transformation numérique de la science, de la société et de l'économie.

Attention: Les candidatures doivent être déposées en ligne sur le site Inria. Le traitement des candidatures adressées par d'autres canaux n'est pas garanti.

Consignes pour postuler

Sécurité défense :
Ce poste est susceptible d'être affecté dans une zone à régime restrictif (ZRR), telle que définie dans le décret n°2011-1425 relatif à la protection du potentiel scientifique et technique de la nation (PPST). L'autorisation d'accès à une zone est délivrée par le chef d'établissement, après avis ministériel favorable, tel que défini dans l'arrêté du 03 juillet 2012, relatif à la PPST. Un avis ministériel défavorable pour un poste affecté dans une ZRR aurait pour conséquence l'annulation du recrutement.

Politique de recrutement :
Dans le cadre de sa politique diversité, tous les postes Inria sont accessibles aux personnes en situation de handicap.