3iA Côte d'Azur
Interdisciplinary Institute for Artificial Intelligence

Ph.D. research topic

- Title: **AI-based precision oncology to monitor response of metastatic cancer to immunotherapy using PET/CT imaging.**
- Research axis of the 3IA: **Axe 2**
- **Supervisor: Olivier HUMBERT**, University professor - Hospital practitioner, iBV and Antoine Lacassagne Center, UniCA, Nice, olivier.humbert@univ-cotedazur.fr
- **Co-supervisor**: **Marco Lorenzi**, tenured research scientist, Epione team, Inria, marco.lorenzi@inria.fr
- The laboratories:
    - PET/CT imaging for precision Oncology team, iBV, Medical School of Nice (http://ibv.unice.fr/research-team/humbert/)
    - EPIONE team, Inria, Sophia-Antipolis (https://team.inria.fr/epione/en/team/marco-lorenzi/)

Apply by sending an email directly to the supervisor, including:

- Letter of recommendation of the supervisor indicated above
- Curriculum vitæ.
- Motivation Letter.
- Academic transcripts of a master's degree(s) or equivalent.
- At least, one letter of recommendation.
- Internship report, if possible.

- **Description of the topic:**

As this is an interdisciplinary "AI and medicine" project, co-supervision by a doctor and a statistical/machine-learning researcher is planned (iBV / Inria)

1- Context and Objective:

Monitoring tumor response using clinical imaging, such as CT or FDG-PET, has become a challenge in the field of immunotherapy, due to atypical evolutive patterns such as pseudo-progression and dissociated response. Standard response criteria such as RECIST or PERCIST are not adapted to the biological basis of immune checkpoint inhibitors. New, specific response criteria are needed, considering the complex morphological and biological evolutive patterns of tumor lesions after immunotherapy initiation. To this end, researchers are focusing on the development of new data-driven approaches integrating imaging information and patient physiological characteristics to improve the simulation and prediction of true therapeutic failure from an inflammatory response. To achieve accurate predictions of

treatment response, we must account for the complexity of the anatomical and biological patient's profile. Beyond imaging biomarkers, this task requires the integration of other complex healthcare data, ranging from biological to clinical features.

The integration of such heterogeneous information within a coherent computational model is currently challenging, due to the typical large dimension and complexity of biomedical data, and the relative low sample size available in typical clinical studies. Consequently, while machine learning approaches often lack of robustness and biological interpretability, mechanistic simulation methods are usually not scalable to account for the large dimensionality of this kind of data.

This project aims to develop new anatomical and functional whole-body atlases of the different evolutionary patterns of response assessed on longitudinal consecutive PET/CT images of patients treated with immune-checkpoints inhibitors. Our final clinical goals are to help to generate new data-driven tumor response criteria, specifically adapted to immunotherapy, so as to optimize the current therapeutic strategy. Specific atypical time-varying patterns such as pseudo-progression and dissociated response will be considered.

2- Methods:

We will focus on the study of **novel inference schemes** allowing to prescribe biologically informed priors as solution of a spatio-temporal modeling problem, for example by developing novel approaches to constrain learning-based models by mechanistic priors. Thanks to the proposed theory, we will investigate the use of simulations informed by such mechanistic approaches to identify differential tumor evolutive patterns and treatment outcomes based on baseline patients' profile.

Finally, we aim at **enriching spatio-temporal treatment response models** accounting for multiple imaging modalities (PET – CT) along with clinical and biological informations. Typical data-driven approaches are characterized by lack of interpretability and scalability problems, due to the complexity and high dimensionality of imaging and biological information. An additional challenge we aim to tackle is represented by the lack of a well-defined temporal reference for the dynamics, and to the geometrical variability in imaging data.

<u>During the project, the candidate will:</u>

- Exploit an existing clinical database containing numerous follow-up FDG/PET exams
- Develop modeling methods for the time-series analysis of PET-CT data
- Develop a methodological formalism for integrating heterogeneous biomedical data
- Gather knowledge in advanced statistical learning methods
- interact with the researchers and medical teams of Inria and Lacassagne Hospital
- Interact with other students and participate to scientific life of the teams.

3- Profile and skills required

We are looking for a candidate with competences in Artificial Intelligence models, medical image processing, and mathematical modeling (Master 2 level).
We seek solid programming and IT skills, along with good communication abilities and an appetite for interdisciplinary work (AI applied to healthcare).