GRENOBLE | MODANE

Proposal for a Master 2 internship – 2026

LPSC, Grenoble

" Modeling of cell survival in targeted alpha therapy: comparison with experimental data and study of cell morphology "

Subject description:

Background: targeted alpha therapy (TAT) uses the injection of vector molecules associated with an alpha particle-emitting radionuclide. It is of particular interest for treating patients with invasive or metastatic cancers. Personalized dosimetric studies are necessary for the clinical optimization of TAT in terms of efficacy and potential toxicities. The very short range of alpha particles (< 100 µm) and the vector biodistribution induces a great heterogeneity of energy deposition at the cellular and tumor scale which can impact treatment planning. This requires the development of adapted tools that can provide information beyond the absorbed dose, which is a challenge due to the multi-scale nature of the data. A research program has been developed in collaboration with several teams of physicists and biologists to address this challenge by proposing an approach for predicting biological efficacy adapted to preclinical studies, supported by biological experiments and high-resolution imaging. The first phase consists of evaluating the biological effects of TAT at the cellular level, through *in vitro* experiments (irradiation of cells in culture wells) with controlled irradiation parameters, and reproducing numerically these irradiations to validate the developed computational chain. The internship work is part of this phase.

Methods: We will use a modeling chain (Grenoble-Lyon collaboration), based on Geant4 Monte Carlo simulations and python analysis associated with the NanOx biophysical model, capable of predicting cell survival for a given irradiation configuration. Clonogenic cell survival measurements will be carried out in Caen with two types of cell lines irradiated with $^{223}Ra\text{-}Cl_2$ and whose irradiation is controlled using an experimental device providing the energy spectrum, the spatial distribution of the isotopes in the culture wells and the dose delivered to the cells. The student will not be in charge of the experiments, but of their numerical reproduction. The numerical evaluations carried out so far, both for the prediction of cell survival and the reconstruction of the dose measured *in vitro*, have been carried out with simplified cell geometries of spherical or ovoid base. However, the size and morphology of the cells can impact these reconstructions. We have therefore produced 3D models of realistic cells imaged by microscopy, segmented and reconstructed (LIRIS collaboration) to evaluate the impact of this parameter on the calculated dose and cell survival.

Internship work:

The internship work will consist of taking charge of the calculation chain and the analyses (with the simplified cell geometry), reproducing by Geant4 simulation the cell irradiations carried out in Caen with ^{223}Ra, and calculating the associated doses and cell survivals in order to compare them with the experimental results. This step aims at linking the doses to the observed biological effects, and thus to constrain the survival prediction model. To study the impact of cell morphology, the student will work on the implementation of the reconstructed cell geometries (from microscopy) in the Geant4 simulation chain. The expected result is the quantification of the differences obtained in terms of absorbed dose and calculated cell survival between the different cells of the same line (approximately 5 to 10 available/line) and between 2 different cell lines, compared to the simplified geometry. The

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analysis will initially concern the CHO-K1 and MDA-231-Br cell lines, of interest to the project, but up to 6 lines are available depending on the progress.

Student profile:

The student should have a good knowledge of nuclear physics and radiation-matter interactions, as well as programming skills (Python, C++). Experience with Monte Carlo simulation and knowledge of (or a strong interest in) radiobiology and radiotherapy are important assets. Due to the collaborative nature of this project and the exploratory nature of the subject, the student should demonstrate a high level of autonomy and interpersonal skills. A good level of English for reading and writing scientific articles is preferred.

Internship location and direction:

Location: Equipe Physique nucléaire et applications médicales, Laboratoire de Physique Subatomique et Cosmologie (LPSC), 53 av. des Martyrs, 38026 Grenoble cedex
Direction : **Rachel Delorme** (LPSC), rachel.delorme@lpsc.in2p3.fr
Co-supervision – collaboration: Part of a project in collaboration with IP2I (Lyon, E. Testa, M. Beuve, M. Alcocer), LIRIS (H. Ladjal), as well as GANIL (A.M. Frelin-Labalme) and ISTCT in Caen. We will do regular (video) meetings with these colleagues. Missions may be possible in Lyon.

Internship duration: 6 months between February 1st and August 31st, 2026, to be determined with the student.

Compensation: Yes, Labex PRIMES grant. Amount according to new regulations in January 2026 (~€600-650/month).

Possibility of pursuing a PhD: A PhD may be considered, according to the student adequation and provided funding is obtained (ED competition).

Application: Send a CV, a cover letter, and transcripts from previous years to rachel.delorme@lpsc.in2p3.fr