POST-DOCTORAL RESEARCH POSTION

Computer modelling of brain cancers by multicellular simulation

IEMN and CANTHER Laboratories, University of Lille

As part of a project at the interface between biology and physics, we are interested in a class of brain tumours representing the first cause of death from cancer in children. Among these, DIPGs (Diffuse Intrinsic Pontine Glioma) are paediatric gliomas with the poorest prognosis. Despite promising results in pre-clinical models, many therapy trials have proved unsuccessful in the clinic, and radiotherapy remains the reference treatment for these tumours. This state of affairs reflects a certain inadequacy of current pre-clinical models in reproducing the biophysical microenvironment of paediatric gliomas, and thus their response to treatment.

In this interdisciplinary project, we are developing a tumour-on-chip microsystem mimicking the micro-environment of these gliomas in terms of their biophysical and biochemical characteristics. The geometry of our biochip allows us to recreate hypoxic zones; the integration of a blood-brain barrier (BBB) will be ensured by the microfluidic connection of a validated functional human model.

In order to understand the biophysics of paediatric gliomas and their heterogeneous response to therapies, the microsystem on chip will be integrated by **high-level mathematical modelling**, aimed at reproducing, characterizing and guiding the experimental system. The topology of the cellular physical environment and the geometry of cellular interactions have an important impact on cellular behaviour. Cultures of cancer cells in a 3D microenvironment with a relevant extracellular matrix mimic the original tissue context, and this allows for better predictive efficiency of preclinical 3D models. We are developing a multicellular agent-based model (ABM), building on our previous work on 3D tumour spheroids, already including a basic description of nutrient diffusion and metabolism and oxygen. This existing mathematical model [1,2] will serve as a basis for the development of a specific multicellular biophysical model, coupling pharmacokinetics and spatial localization, for an idealized BHE-DIPG system. Metabolites that are identified as essential for DIPG survival will be included, through sets of partial differential equations (PDEs) to couple nutrient metabolic cycling, O_2 consumption, and cellular parameters.

More information about the participating teams can be found at:
https://www.iemn.fr/la-recherche/les-groupes/physique
https://www.iemn.fr/la-recherche/les-groupes/biomems
http://canther.fr/fr/equipe-plasticite-cellulaire-et-cancer/

The post-doc researcher to be recruited will work on the development of the simulation model algorithms, their computer implementation, the parameterization based on experimental data, as well as the development of detailed simulations in support of the experimental activities to be carried out on the system. tumor-on-chip. Alongside this main theoretical activity, he/she may also participate in setting up and monitoring certain parts of the experimental program.

The profile sought is that of a doctorate/PhD holder in physics, chemistry, mathematics, or biology, with demonstrated capabilities in computer numerical modelling for biophysics; familiarity with Linux/Unix operating systems; Python, C/C++, Fortran programming skills.

24-month work contract not-renewable, with salary determined by the CNRS age/experience parameters.
Main work site: Laboratoire Central of IEMN, 59650 Villeneuve d'Ascq (France)
Candidates must include: detailed CV; at least two references (person susceptible of being contacted by phone or e-mail); a one-page motivation statement; a one-page summary of the PhD thesis.
Send your application to: fabrizio.cleri@univ-lille.fr.

[1] M Tomezak, C Abbadie, E Lartigau, F Cleri, A biophysical model of cell evolution after cytotoxic treatments: Damage, repair and cell response, *J Theor Biol* **389**, 146 (2016)
[2] F Cleri, Agent-based model of multicellular tumor spheroid evolution including cell metabolism, *Eur Phys J E* **42**, 112 (2019)