avec le Fonds européen de développement régional (FEDER)

BioImp - Microtechnologies for innovative therapy

Post-doctorate - Assesment of cell-cell interaction

• Contract type :	Post-doctorate - temporary position
• Duration :	2 years
• Location :	Institut FEMTO-ST, Besançon, France
• Starting date :	June - December 2025
• Contact :	bioimp.recrutement@femto-st.fr
• Funding :	(ERDF BioImp project), funded by the European Union (17.8 M€)
• Employer :	Université Marie et Louis Pasteur

I Context

The FEMTO-ST research institute (CNRS) innovates in cutting-edge technological solutions for the manufacture of biomedicines (drugs whose active ingredient is of biological origin), calling on a multidisciplinary team with skills in robotics, automation, computing, microfluidics, microsystems and clean-room manufacturing. We're looking for curious people with a good scientific background wanting to thrive in the world of research and innovation.

II Job description

The production of biopharmaceuticals requires the ability to move biological cells in a controlled manner. Among the various manipulation methods, non-contact manipulation methods using force fields [8] allow interaction with biological objects without direct contact. This avoids all issues of biological contamination, ensuring the sterility of the cells and the liquid environment in which they are cultivated.

The goal of this position is to develop a device able to quantify the interactions between lympocytes and tumour cells, and analyze the immune synapse that is formed when the contact is made.

Classical approaches used to assess cell avidity include qualitative measurements based on fluorescence [6], statistical force estimation obtained by acoustic force spectroscopy [7] or drag flows [1], or force measurement performed at a single cell level by AFM force spectroscopy [2]. Obtaining quantitative data at a single cell level that could be coupled with other information such as fluorescence is still a challenge, as these techniques require long preparation time to attach the cells to the manipulator. An appealing solution is offered by optical tweezers [5]. These instruments use a highly focused laser beam, that can be mounted inside an inverted optical microscope, to apply forces on

objects thanks to the light. For objects such as cells or beads (glass or polystyrene) attractive forces are applied due to the light radiation, meaning that the objects will be trapped by the laser, and can be moved by deviating the laser beam.

Optical tweezers offer the possibility to bring cells in contact, facilitating the analysis of the interaction by imaging and fluorescence approaches [4]. Optical tweezers can even be used to perform quantitative force measurement. These systems can measure forces in the order of pN, up to hundreds of pN. They have been very recently used to evaluate anti-integrin antibodies as potent inhibitors of the macrophage adhesion to tumor cell targets [3]. We propose in this project to use optical tweezers to evaluate qualitatively and quantitatively the immune synapse of CAR-T cells and their adhesion kinetics. This system will provide live visual information of the experiment through an inverted microscope, the force applied on the cells in Newton, and fluorescence information so that force estimation can be confronted with other modalities. We expect to analyze the interaction of a few cells per minute, as the limiting factor is the time needed for the interaction establishment between lymphocytes and target cells, during which it is necessary to hold them in contact. Experiments will be conducted inside a temperature controlled fluidic chip with up to 5 inlets to bring cells and medium into the main chamber.

The development of this device represents both a technical and scientific challenge. It would enable the study of cellular interactions, improve the productivity of innovative therapeutic drugs, and enhance their accessibility.

III Tasks

In the context of this position, you will be required to conduct both theoretical studies (for modeling various physical phenomena and performing simulation studies) as well as experimental studies requiring the design and development of optical, electrical and mechanical systems, the implementation of control algorithms, and data analysis. You will also need to handle biological objects and work in a cleanroom environment. You will be part of a team of engineers, post-docs, PhD students, researchers, and faculty members with complementary expertise on which you can rely.

Basic equipment for the manipulation of cells are available (Biological Safety Cabinet, incubator, fridge, ...). One of the partner of the project (the french blood agency EFS) will provide the biological cells. As the two labs are situated in the same city (separated by less than 8 kilometers), easy exchange of biological material will be possible.

In more detail, the tasks you will be required to perform are :

- Study existing methods in the literature for assessing cell interactions with optical tweezers and impedance measurement
- Define the protocols to analyze cell interactions using optical tweezers and impedance measurement
- Design and fabricate a home-made chip for impedance measurement
- Propose an efficient control law enabling testing multiple cells simultaneously
- Design an experimental setup (mechanical, electronic, and programming components) and microfluidic chips

IV Skills

We're looking for someone with a PhD in robotics, automation, physics or microfluidics.

The following skills are not mandatory but would be an asset for the candidate :

- Knowledge of biology
- Knowledge of electrostatics and a good understanding of Maxwell's equations
- Modeling and control of non-linear systems
- Experience in microfluidics
- Experience of optical tweezers

V Work environment

FEMTO-ST is a multidisciplinary research unit associated with the CNRS. It is one of the largest science and technology laboratories in France (750 researchers), with a wide range of scientific skills and, in particular, internationally recognised know-how in the field of micro robotics and small-scale manipulation and characterisation. The post will be based in an exceptional environment:

- The cleanroom microfabrication technology centre, MIMENTO, will be used to manufacture the microdevices for this project. It is managed by a technical team of around fifteen engineers and technicians. It has a total area of around $1300m^2$, including $865m^2$ of clean room space (ISO class 5 to 7). It is part of the Renatech network, which brings together the 5 largest French centres for microtechnology research.
- The Micro and Nano Robotics Centre (CMNR) offers unique access to manipulation and characterisation facilities for small-scale manufacturing, assembly and characterisation. In particular, the fluid chip micromanipulation station will be used to carry out all the experimental developments required for the project.
- Strong partnerships: The Bioimp project is made up of a multi-disciplinary academic and industrial consortium from the health and microtechnology sectors (EFS, CellQuest, RD Biotech, Diaclone, Med'Inn'Pharma, the RIGHT and FEMTO-ST laboratories at the Université Marie et Louis Pasteur and FC'innov)
- A dedicated project team: the person recruited will be supervised on a day-to-day basis by 1 or 2 researchers/teacher-researchers, and will be part of a project team comprising 5 researchers/teacher-researchers and around 7 engineers/post-doctoral students directly involved in the project.
- An International working environment (ability to speak French is not require) in a pleasant town connected to major cities (2 hours from Paris by TGV, 1 hour from Dijon by train, 2 hours from Lausanne and Lyon)

Références

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