PhD thesis offer within the OptiReac4MSC Project

Optimisation of stirred tank bioReactor design and operation for the culture of Mesenchymal Stem Cells adhered on microcarriers

A **4-year PhD position** is currently available in the Department of Chemical Engineering at the University of Liège (Belgium). This offer is done in the context of the OptiReac4MSC project funded by the FNRS.

Research area:

Potential applications of mesenchymal stem cells (MSCs) in medicine are very numerous, particularly in the fields of cell therapy, thanks to their immunosuppressive and anti-inflammatory properties. They are therefore identified as the basis of the next medical revolution and many clinical trials are currently underway. For example, due to their properties, stem cells are currently considered as a very promising route to prevent the severe acute respiratory infection form of COVID-19.

Unfortunately, the amounts of MSCs sampled from a donor are very small compared to the quantities necessary for a therapeutic treatment. An *in vitro* expansion step is therefore essential. The cultivation of MSCs on microbeads (microcarriers) in closed and controlled stirred tank type bioreactors is seen as the most promising in-vitro expansion process. The applicability of this technology to MSC culture has been demonstrated, but culture conditions still need to be optimized to maximize MSC production while maintaining their quality and functionality. In particular, it is required to **design specific stirred bioreactors** ensuring the complete suspension of microcarriers, while keeping hydromechanical stresses as limited as possible.

Description of the tasks:

The main aim of the project is to develop and validate a detailed hydrodynamic model describing the microenvironments encountered by mesenchymal stem cells (MSC) grown on microcarriers in a mechanically stirred bioreactor with a focus on the hydromechanical stresses undergone by MSC. It will quantify the link between (1) the choice of design and operating conditions of the bioreactor and (2) the distribution of spatiotemporal hydrodynamic conditions prevailing within it. The prediction capability of this tool in terms of solid spatial distribution and hydromechanical stresses will be assessed, both during the steady-state phase of suspension and the transitional phase when the microcarriers are resuspended after microcarrier addition and agitation restart. To choose the appropriate models to simulate such complex flow, a better understanding of the liquid-solid and solid-solid interactions, i.e. how the solid phase influences the liquid phase and vice versa, is necessary.

The project is divided in three main parts. The first part is dedicated to the experimental characterization of the liquid-solid flow in a stirred tank bioreactor in terms of solid spatial distribution and of mean and turbulent quantities using light attenuation and PIV techniques. Collisions between particles will also be studied experimentally using a time-resolved camera. The experimental data acquired will be the basis for the development and the validation of the numerical tool that will be developed during the second part of the project.
Finally, in the third part, the numerical approach will be used for the characterization of various bioreactor designs and operating conditions to study their influence on the hydromechanical stresses and help define design and scale-up rules for the optimization of stem cell cultures in stirred tank bioreactors.

Candidate's profile:
Candidates must have a Master's degree in Chemical or Mechanical Engineering or similar fields (process or environmental engineering…). A strong background in Fluid Mechanics is required and candidates should have a strong interest in both experimental and numerical characterization of multiphase flow hydrodynamics.
Previous experience with CFD code such as Ansys Fluent software (or similar) as well as numerical programming (Python, Matlab…) is a plus.
Ease to communicate in English (oral and written) is required, French is an additional asset.

Research environment:
The successful candidate will join a dynamic team (PEPs, Products Environment and Processes- within the Department of Chemical Engineering (DCE) of the University of Liège. The DCE employs about 60 people, with more than 10 different nationalities, mostly active in the fields of chemical and process engineering and materials science.
The promoter team is specialized in the fields of (bio)chemical reaction engineering and multiphase flow systems, with senior researchers recognized for their competencies both in academia and in industry.
The experimental part of the research will be done in the Halle de Génie chimique which is a 900 m^2 experimental hall including an analytical laboratory, an electrical and a mechanical workshop as well as a number of rooms dedicated to outstanding experimental equipment (PIV-PLIF, optical trajectography, X-ray tomographs) or bench scale apparatus (stirred tanks, packed columns, photobioreactors).
The numerical part will benefit of the licenced (Matlab, Ansys-Fluent, Dynamic Studio) and of "in house" codes (Lattice-Boltzman, hydrid stochastic CFD-based compartment model, tomographic reconstruction and image analysis algorithms…) available in the Department as well as of powerful workstations.

Moreover, the promoter has established a long-lasting collaboration with a French research team (CNRS/LRPG/BioProMo, Nancy) working on the development and optimization of animal/stem cell culture processes. They are currently involved in the Interreg project ImproveStem (2017-2021 - https://improve-stem.com/) and in an on-going thesis (2019-2022) under joint supervision between the University of Liege (Pr D. Toye) and the University of Lorraine (Pr E. Olmos and Pr N. de Isla).

More information about the Department of Chemical Engineering:
www.chemeng.uliege.be

One professor and one senior researcher will be in charge of mentoring this PhD thesis:
Prof. Dominique TOYE, active in the field of reactors design and modeling. See publications:
https://orbi.uliege.be/simple-search?query=dominique+toye

Dr. Angélique DELAFOSSE, active in the field of experimental and numerical characterization of multiphase flow. See publications:
https://orbi.uliege.be/simple-search?query=delafosse

Recruitment process:
Applications containing CV, cover letter and possibly reference letters should be submitted by e-mail to secretary.chemeng@uliege.be with in object the mention "Application PhD thesis OptiReac4MSC ". Application deadline is January 25th, 2021.

Candidates selected from this first round will be invited for an interview (possibly through Visioconference) during which they will be asked to briefly present a previous topic they worked on.

The successful candidate will receive a PhD student position for a 4-year period. The grant amount is in accordance with university standards (~1800 €/month, net).

Start of the PhD should ideally take place before March 1st, 2021.