MSc project: Development of a 3D cell tracking model for studying cancer cell migration

Introduction

Cancer research has long relied on two-dimensional (2D) cell culture models for studying tumour biology and drug responses. However, these models often fail to recapitulate the complexity of the tumour microenvironment (TME). Three-dimensional (3D) cell culture systems can be employed to address this limitation, as they are able to more accurately mimic *in vivo* physiological conditions [1]. Microfluidic-based platforms have proven to be a powerful tool for creating these 3D systems, and allow control over environmental factors such as fluid flow and substrate stiffness, making them an ideal for studying tumour progression and therapeutic responses *in vitro* [2].

Objective

In this interdisciplinary project, we would like to develop tumour cell aggregates, called spheroids, integrated within a microfluidic chip. This microfluidic system will incorporate controlled shear flow conditions and real-time imaging. The tumour cells from the aggregate migrate into the surround 3D matrix, a hydrogel, and break it down (see Figure 1). The main objective of this student project is to define these migratory patterns. Establishing the paths these cells follow via cell tracking, would allow us to study the effect of external factors such as fluid flow, matrix stiffness and porosity.

Your role in this project

This master student project offers an opportunity to contribute to the development of innovative tools for cancer research. Your goal will be the development of a cell tracking script to quantifying cancer cell migration via image analysis. This is to be achieved via two main steps: segmentation and tracking. Potentially utilizing artificial intelligence (AI) techniques. This will allow for subsequent analysis of the cell migration path in terms such as cell displacement, acceleration, angle, persistence, and velocity. This project represents a significant advancement in the field of cancer research, which focusses on providing a more accurate and physiologically relevant model for studying tumour behaviour and therapeutic responses.

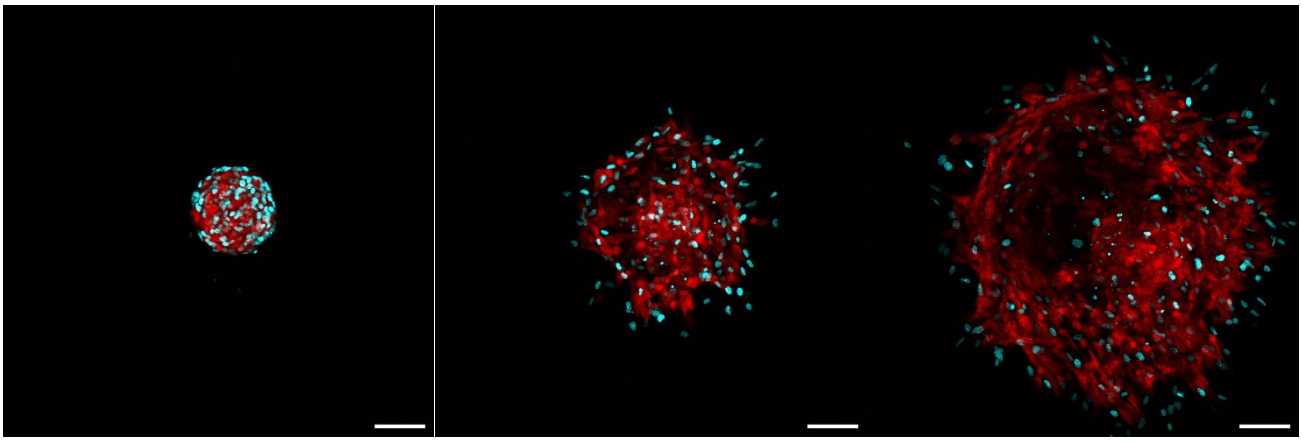

Figure 1. Spheroid consisting of two different cell types. The spheroid contained cancer cells (red) and fibroblasts (blue), and were suspended in a fibrin hydrogel. The images were obtained via confocal fluorescence microscopy, and were taken as a z-stack and represented here in a max intensity projection. At t=0, the cells clustered together (A), after which they migrated outwards, imaged here at t=20h (B) and t=40h (C). Scalebar is 100 µm.

For inspiration, see the following links

- Interstitial flow potentiates TGF-β/Smad-signaling activity in lung cancer spheroids in a 3D-microfluidic chip†
- 3DeeCellTracker, a deep learning-based pipeline for segmenting and tracking cells in 3D time lapse images
- Computerized cell tracking: Current methods, tools and challenges

Required experience

- Coding (Matlab, Python)

Duration of the project

- 4-6 months

Contact information

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References

[1] C. Jubelin *et al.*, "Three-dimensional in vitro culture models in oncology research," *Cell Biosci*, vol. 12, no. 1, Dec. 2022, doi: 10.1186/S13578-022-00887-3.

[2] Y. H. V. Ma, K. Middleton, L. You, and Y. Sun, "A review of microfluidic approaches for investigating cancer extravasation during metastasis," *Microsystems & Nanoengineering 2018 4:1*, vol. 4, no. 1, pp. 1–13, Apr. 2018, doi: 10.1038/micronano.2017.104.