PhD PROJECT PROPOSAL

## **PhD Project Title**

Topological Data Analysis for Predictive Spatial Signatures of Cancer Progression and Treatment Response

## **PhD Supervisory Team**

Principal Supervisors: Dr Fabian Spill, f.spill@bham.ac.uk, Mathematical Biology, School of Mathematics

Industrial Supervisor: Arthur Lewis, AstraZeneca

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## **Project Abstract**

Cancer remains a major killer, still rarely curable in advanced stages. Recent experiments revealed a high complexity in terms of a huge number of perturbed molecules (e.g. genes, proteins or metabolites), and also a high disturbance of the spatial patterning of the different cell types in a tumour. Mathematical methods typically focus on characterising one of these complexities. In this project, we will advance methods to reveal the interplay of spatial and high-dimensional molecular signatures through novel mathematical methods based on topological data analysis, network science and spatial statistics.

## **Detailed Project Description**

***Background***

For a long time, cancer has been largely studied through its genetic alterations. However, we now know that other cell types such as immune cells critically affect tumour progression. Moreover, the immune system can be reprogrammed through immuno-therapies that are revolutionising our arsenal of cancer therapies.

Initial studies of the role of immune cells in cancer simply counted certain immune cells, such as T-cells or macrophages, within the tumour. Inspecting large data sets of multiplexed fluorescent allows one to visualise many different cell types simultaneously, and reveals that these immune cells appear in complex patterns within tumours. Similarly, spatial mass spec data reveals a high level of heterogeneity of molecular signatures within a tumour.

**Outcome**

In this project, the PhD student will develop a new workflow based on topological data analysis to uncover spatial signatures that characterise different stages of tumour progression and that are predictive of the response to cancer therapy. They will combine spatial methods with methods to integrate different data types to utilise special multi-omics data from tumours, obtaining a holistic view of a tumour that incorporates spatial and molecular heterogeneity. The student will establish new biomarkers based on the spatial, multi-omics and topological characteristics of the tumour microenvironment that will underpin optimised, personalised treatments.

**Methodology**

The project will combine methods from topological data analysis, spatial statistics and bioinformatics. Specifically, they will advance approaches based on persistent homology, pair correlation functions, network analysis, pathway enrichment analysis, clustering analysis, entropy measures and community detection algorithms to combine information from different data types (cell types, transcriptomics, metabolomics, proteomics, lipidomics etc) to obtain a more holistic view of the spatial patterning of cells in tumours.

**Suitability for CDT and University**

This project fits very well into the CDT due to its employment of core topology techniques (e.g. persistent homology, analysis of networks) and the highly interdisciplinary nature at the interface of mathematics, computer science and biomedicine. This also fits well into the UoB strategy, especially due to the inclusion of AstraZeneca, a key partner of the university.