Doctoral Thesis Summary

This thesis investigates brain tumour growth through advanced mathematical models that integrate mechanical deformation, phenotypic heterogeneity, and fluid-nutrient transport. By employing multiscale and multiphase approaches, the research captures tumour dynamics and their impact on surrounding brain tissues, paving the way for patient-specific therapeutic strategies.

Malignant brain tumours represent a significant challenge in modern medicine due to their aggressive behaviour, resistance to treatment, and unpredictable locations. Despite advancements in clinical research, recurrence remains the primary cause of mortality. Tumour migration and invasion into brain tissue involve complex, poorly understood mechanisms, highlighting the necessity of mathematical models to deepen our understanding of these processes.

The thesis begins with an introduction in *Chapter 1*, which examines the biological characteristics of tumours, with a focus on brain tumours. This includes a discussion of tumour grades and their defining features. From a mathematical standpoint, the chapter provides a general overview of modelling approaches and introduces the framework employed throughout this work.

Chapter 2 presents a multiphase mechanical model that quantifies tumour-induced deformations and stresses. By incorporating anisotropic growth driven by brain fibre orientations, the model captures the irregular and heterogeneous behaviour of tumours. Patient-specific MRI and DTI data enable the reconstruction of realistic 3D brain geometries, facilitating simulations of ventricular compression and its effects on adjacent healthy tissue. The model also incorporates therapeutic scenarios, such as chemotherapy and radiotherapy. Numerical results, computed using FEniCS, demonstrate the model's ability to replicate the mechanical impact of tumour growth and provide insights for personalised therapeutic strategies.

Chapter 3 investigates the viscoelastic behaviour of brain tissue using ramp-and-hold relaxation tests in torsion performed on freshly harvested cylindrical ovine brain samples. The complete set of viscoelastic parameters is estimated through a simultaneous fit to analytical expressions for torque and normal force predicted by the modified Quasi-Linear Viscoelastic (MQLV) model. Finite element simulations in FEniCS validate the model's predictions, showing excellent agreement with experimental data. The derived parameters have broader implications, including applications in traumatic brain injury research and the development of protective sports headgear.

Chapter 4 explores cancer cell dynamics and immune system interactions in the context of immunotherapeutic treatments involving T-lymphocyte infusions. An ordinary differential equation (ODE) model identifies critical thresholds for therapy effectiveness through bifurcation analyses. Building on this, a partial differential equation (PDE) model incorporates spatial dynamics via diffusion and chemotaxis, allowing simulations of tumour growth and immune responses within 3D patient-specific brain geometries. Sensitivity analyses provide valuable insights into tumour-immune dynamics, supporting the design of personalised immunotherapeutic interventions.

Chapter 5 examines phenotypic heterogeneity in tumour cells under varying oxygen conditions using a reaction-diffusion partial integro-differential equation (PIDE) framework. The model accounts for anisotropic diffusion, capturing the directional influence of the extracellular environment. Numerical simulations reveal complex wavefront dynamics driven by spatial variations in oxygen and phenotypic traits. Applications to 3D brain geometries reconstructed from MRI and DTI data elucidate the interplay between tumour growth, oxygen diffusion, and cell migration along white matter tracts, advancing the development of patient-specific therapies.

Chapter 6 introduces a PDE-based model for fluid and nutrient transport within the tumour microenvironment. Using asymptotic homogenisation, the model integrates microscale vascular details into a double porous medium framework, coupling fluid dynamics with nutrient transport. Permeability and diffusivity tensors derived from cell-problem analyses encapsulate the influence of microvascular geometry on macroscopic behaviour. The Kedem-Katchalsky formulation describes nutrient and fluid exchange across capillary walls. While limitations remain, the framework provides a basis for numerical simulations of realistic tumour geometries and supports the development of anti-cancer treatments.

This thesis bridges experimental, clinical, and computational approaches, offering innovative mathematical methodologies to advance the understanding of brain tumour growth and progression. The findings lay the groundwork for future research and contribute to the development of mathematical models capable of incorporating patient-specific anisotropic data and personalised treatments, with the potential to significantly improve patient outcomes in oncology.