

Mathematical Modeling of Glioblastoma: Stem Cell Dynamics, Therapy and Digital Twins

Nicholas Harbour - The University of Nottingham

Brain cancer remains one of the deadliest forms of cancer, with survival rates showing little improvement over the past two decades.

Treatment is uniquely challenging due to the fast-growing and highly diffuse nature of brain tumours. Current clinical practice largely follows a “one-size-fits-all” approach, with limited patient-specific personalisation, despite the substantial heterogeneity observed between patients.

I develop data-driven mathematical models that simulate brain tumour growth and response to treatment. These models, sometimes referred to as digital twins, consist of systems of equations that encode biological knowledge of cellular interactions during tumour progression and therapy. By fitting these models to patient data, we can generate personalised virtual tumours capable of predicting individual disease trajectories and treatment response.

Using this framework, I assessed the therapeutic potential of a novel differentiation-based therapy, BMP4, for brain cancer. Although BMP4 has shown promise, its translation to clinical impact has been hindered by highly heterogeneous responses across experimental systems. By integrating new preclinical data into the mathematical model, I quantitatively captured patient-specific variation in BMP4 sensitivity. I then simulated a series of virtual clinical trials accounting for this observed heterogeneity.

The simulations indicate that conventional trial designs are unlikely to detect meaningful benefit in unstratified patient cohorts. However, incorporating clinically feasible patient pre-selection strategies based on model-derived biomarkers is predicted to substantially improve treatment efficacy and patient outcomes.

This work demonstrates how mathematical modelling can be used to guide personalised treatment strategies, ensuring that the right therapy is delivered to the right patient.

