MAT292 Proposal:
Comparing Classical and Neural ODEs in Predicting the Growth of Glioblastoma Tumours

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1 Project Goal

We aim to compare neural ordinary differential equations (ODEs) with classical models for predicting the growth of glioblastoma tumours using MRI images. The machine-learning model ("neural ODE" or "ML model") will be trained on publicly sourced MRI data, and its results will be compared with the classical models to determine the validity and accuracy. Furthermore, we will analyze the bifurcations of glioblastoma models and how tumour sizes affect their growth. If possible, we will further determine how modifications can be made to the ML model or preprocessing steps to yield better results, thereby enhancing the model accuracy for this incurable condition.

More specifically, we will split the publicly sourced MRI data into training and testing sets. The ML model will be trained using the training sets. The ODEs will be evaluated using the testing set, using numerical methods, specifically the Runge-Kutta fourth-order method and the Levin method, to maintain computational accuracy and runtime [6] [3]. The prediction accuracy of the neural ODE will be determined by comparing its performance with the classical models on the testing set. They will provide a benchmark for performance and computational efficiency.

2 General Background

Glioblastoma—a neoplastic growth of the glial cell—is the most common and aggressive form of brain tumour [2]. Like other tumours, it uses chemotaxis, the directed movement of cells or organisms in response to a chemical gradient, which largely influences tumour growth speed and metastasis. It spreads rapidly and is incurable. Thus, the only possible course of action is to reduce symptoms and slow their growth. Glioblastoma tumours are classified based on the width of tumour rings and tumour surface regularity, which assesses the extent to which a tumour resembles a sphere [11]. Spherical tumours indicate slower progression compared to 'spikey' tumour surfaces [7]. These factors alter the survival rate of patients, and the correlation can be predicted using PDEs, ODEs, or ML models.

3 Background Math

ODEs and partial differential equations (PDEs) help determine the evolution rates of tumours and how factors like glucose levels, chemotaxis, chemo-radiation, and different treatments can perturb the proliferation of the cells. A PDE for modelling cancer cells is:

$$\frac{\partial c}{\partial t} = \nabla \cdot (D \nabla c) + \rho c - G(t)c \tag{1}$$

Here, D is the diffusion coefficient (the rate of water diffusion through a tumour's microenvironment), ρ is the net proliferation rate (how fast cells grow and divide), and c is the cell density at a particular time and location [13]. G(t)c is a constant added to the otherwise general equation that determines the number of dead tumour cells from various chemotherapy treatments, providing a 'heterogeneous drug administration' approach [12]. We can use Equation (1) to model the inverse trend between the cellularity of tumours and the diffusion coefficients in various tissues.

3.1 Carrying Capacity

The Gompertz model describes tumour growth as experiencing an 'initial exponential growth' before inflecting as it reaches a carrying capacity/maximum size [9]. However, a stochastic differential equation was used to represent this behaviour instead of a PDE as it better accounts for varying uncertainty and randomness based on individual patient health. In a study related to glioblastoma, the stochastic differential model in Equation (2) notes an inverse relationship between tumour volume and 'specific growth rate' (SGR) [12], and incorporates it into the Gompertz Model, as seen below [10].

$$dV = aV \log\left(\frac{b}{V}\right) dt + \frac{cV}{h + \sqrt{V}} dW(t) \tag{2}$$

Here, a(V) is the intrinsic growth rate, V is the tumour size, the term $\frac{cV}{h+\sqrt{V}}$ accounts for white noise or randomness from the MRI data, and W(t) assesses the probability distribution [1]. The Gompertz curve is incorporated within the term log $\frac{b}{V}$, where b is the carrying capacity of the cancer, as cells are depleted from blood, glucose and oxygen supplies.

3.2 Bifurcation Model

Bifurcation models assess the relation between tumour and non-tumour cells using nonlinear ODEs [8]. As the ODE models discussed above have multiple parameters, both 'Codimension 1' and 'Codimension 2' bifurcations must be examined. Bifurcation analysis helps us inspect how interactions with effective cells, cells in the immune system responding to these tumours, can spark invasion, proliferation or cell inaction within the glioblastoma [4]. Possible bifurcations include transcritical saddle-nodes and Hopf bifurcations using center manifold and normal form theories, which will be analyzed in our analysis.

4 Background Neural Network

After examining several models, we chose to use DeepSeg, a deep learning architecture that fully automates the detection and segmentation of the brain with MRIs. This particular model is based on a modified U-Net architecture, which extracts spatial features from MRI scans and reconstructs them into a probability map to highlight tumour regions. It has a DSC (dice similarity coefficient) of 0.81-0.84, making it a clinically useful model for predicting tumour growth [14].

To evaluate the NN in relation to the classical ODEs, we draw inspiration from a similar article [5] that compared classical ODEs to neural ODEs in tumour growth. The methods used are relative bias, mean-squared error (MSE), and relative root-mean-squared error (RMSE), serving as a basis for evaluating the performance of our NN.

5 Scope, Objectives and Milestones

While many of the PDEs and ODEs are used for other cancer cells, we will conduct our analysis specifically considering the growth of glioblastoma cells. We will limit our MRIs to a single database or characteristic within a database to minimize the number of uncontrolled parameters that can vary our results.

Based on similar literature, the comparison of neural and classical ODEs is an area of research within biological system modelling and prediction. Given the relevance of knowing the spread and growth of glioblastoma cells early on for early prevention and administering care to patients, we believe this topic can adequately apply MAT292 concepts to address broader healthcare issues.

The following table outlines our milestones:

Table 1: Project Task Timeline

Task	**Estimated Time**	**Internal Due Date**
Broader literature review to finish our research for relevant models for ODEs and Neural Networks	7 hours	Oct 10
Preprocess images from public data sets, train and test NN, and get performance parameters	7 hours	Oct 17
Apply classical ODEs to the MRIs	7 hours	Oct 24
Compare and analyze each method's result, and conduct specificity analysis	7 hours	Oct 27
Bifurcation analysis	5 hours	Oct 30
Writing, drafting, editing	10 hours	Nov 1

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